



PATENT APPLICATION
Attorney Docket No. 15966-697 (Cura-197)

NOVEL PROTEINS AND NUCLEIC ACIDS ENCODING SAME

RELATED APPLICATIONS

5 This application claims priority from USSN 60/186,592, filed March 3, 2000; USSN 60/186,718, filed March 3, 2000; USSN 60/187,293, filed March 6, 2000; USSN 60/187,294, filed March 6, 2000; USSN 60/190,400, filed March 17, 2000; USSN 60/196,018, filed April 7, 2000; USSN 60/259,548, filed January 3, 2001; each of which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

The invention relates generally to polynucleotides and polypeptides, as well as
10 vectors, host cells, antibodies, and recombinant methods for producing these nucleic acids
and polypeptides.

SUMMARY OF THE INVENTION

The invention is based in part upon the discovery of novel nucleic acid sequences encoding novel polypeptides. The disclosed FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6 and FCTR7 nucleic acids and polypeptides encoded therefrom, as well as derivatives, homologs, analogs and fragments thereof, will hereinafter be collectively designated as “FCTR_X” nucleic acid or polypeptide sequences.

In one aspect, the invention provides an isolated FC₁TRX nucleic acid molecule encoding a FC₁TRX polypeptide that includes a nucleic acid sequence that has identity to the nucleic acids disclosed in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In some embodiments, the FC₁TRX nucleic acid molecule will hybridize under stringent conditions to a nucleic acid sequence complementary to a nucleic acid molecule that includes a protein-coding sequence of a FC₁TRX nucleic acid sequence. The invention also includes an isolated nucleic acid that encodes a FC₁TRX polypeptide, or a fragment, homolog, analog or derivative thereof. For example, the nucleic acid can encode a polypeptide at least 80% identical to a polypeptide comprising the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The nucleic acid can be, for example, a genomic DNA

fragment or a cDNA molecule that includes the nucleic acid sequence of any of SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Also included in the invention is an oligonucleotide, *e.g.*, an oligonucleotide which includes at least 6 contiguous nucleotides of a FCTR_X nucleic acid (*e.g.*, SEQ ID NOS: 1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24) or a complement of said oligonucleotide.

Also included in the invention are substantially purified FCTR_X polypeptides (SEQ ID NO: 2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25). In certain embodiments, the FCTR_X polypeptides include an amino acid sequence that is substantially identical to the amino acid sequence of a human FCTR_X polypeptide.

The invention also features antibodies that immunoselectively-binds to FCTR_X polypeptides, or fragments, homologs, analogs or derivatives thereof.

In another aspect, the invention includes pharmaceutical compositions that include therapeutically- or prophylactically-effective amounts of a therapeutic and a pharmaceutically-acceptable carrier. The therapeutic can be, *e.g.*, a FCTR_X nucleic acid, a FCTR_X polypeptide, or an antibody specific for a FCTR_X polypeptide. In a further aspect, the invention includes, in one or more containers, a therapeutically- or prophylactically-effective amount of this pharmaceutical composition.

In a further aspect, the invention includes a method of producing a polypeptide by culturing a cell that includes a FCTR_X nucleic acid, under conditions allowing for expression of the FCTR_X polypeptide encoded by the DNA. If desired, the FCTR_X polypeptide can then be recovered.

In another aspect, the invention includes a method of detecting the presence of a FCTR_X polypeptide in a sample. In the method, a sample is contacted with a compound that selectively binds to the polypeptide under conditions allowing for formation of a complex between the polypeptide and the compound. The complex is detected, if present, thereby identifying the FCTR_X polypeptide within the sample.

The invention also includes methods to identify specific cell or tissue types based on their expression of a FCTR_X.

Also included in the invention is a method of detecting the presence of a FCTR_X nucleic acid molecule in a sample by contacting the sample with a FCTR_X nucleic acid probe or primer, and detecting whether the nucleic acid probe or primer bound to a FCTR_X nucleic acid molecule in the sample.

In a further aspect, the invention provides a method for modulating the activity of a FCTR_X polypeptide by contacting a cell sample that includes the FCTR_X polypeptide with a

compound that binds to the FCTR_X polypeptide in an amount sufficient to modulate the activity of said polypeptide. The compound can be, *e.g.*, a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic (carbon containing) or inorganic molecule, as further described herein.

Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The Therapeutic can be, *e.g.*, a FCTR_X nucleic acid, a FCTR_X polypeptide, or a FCTR_X-specific antibody, or biologically-active derivatives or fragments thereof.

The invention further includes a method for screening for a modulator of disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma,

malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The method includes contacting a test compound with a FCTR_X polypeptide and determining if the test compound binds to said FCTR_X polypeptide. Binding of the test compound to the FCTR_X polypeptide indicates the test compound is a modulator of activity, or of latency or predisposition to the aforementioned disorders or syndromes.

Also within the scope of the invention is a method for screening for a modulator of activity, or of latency or predisposition to an disorders or syndromes including, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune

effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy by administering a test compound to a test animal at increased risk for the aforementioned disorders or syndromes. The test animal expresses a recombinant polypeptide encoded by a FCTR_X nucleic acid. Expression or activity of FCTR_X polypeptide is then measured in the test animal, as is expression or activity of the protein in a control animal which recombinantly-expresses FCTR_X polypeptide and is not at increased risk for the disorder or syndrome. Next, the expression of FCTR_X polypeptide in both the test animal and the control animal is compared. A change in the activity of FCTR_X polypeptide in the test animal relative to the control animal indicates the test compound is a modulator of latency of the disorder or syndrome.

In yet another aspect, the invention includes a method for determining the presence of or predisposition to a disease associated with altered levels of a FCTR_X polypeptide, a FCTR_X nucleic acid, or both, in a subject (*e.g.*, a human subject). The method includes measuring the amount of the FCTR_X polypeptide in a test sample from the subject and comparing the amount of the polypeptide in the test sample to the amount of the FCTR_X polypeptide present in a control sample. An alteration in the level of the FCTR_X polypeptide in the test sample as compared to the control sample indicates the presence of or predisposition to a disease in the subject. Preferably, the predisposition includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and

granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. Also, the expression levels of the new polypeptides of the invention can be used in a method to screen for various cancers as well as to determine the stage of cancers.

In a further aspect, the invention includes a method of treating or preventing a pathological condition associated with a disorder in a mammal by administering to the subject a FCTR_X polypeptide, a FCTR_X nucleic acid, or a FCTR_X-specific antibody to a subject (*e.g.*, a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, *e.g.*, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders,

neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

In yet another aspect, the invention can be used in a method to identify the cellular receptors and downstream effectors of the invention by any one of a number of techniques commonly employed in the art. These include but are not limited to the two-hybrid system, affinity purification, co-precipitation with antibodies or other specific-interacting molecules.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION

The invention is based, in part, upon the discovery of novel nucleic acid sequences that encode novel polypeptides. The novel nucleic acids and their encoded polypeptides are referred to individually as FCTR1, FCTR2, FCTR3, FCTR4, FCTR5, FCTR6, and FCTR7. The nucleic acids, and their encoded polypeptides, are collectively designated herein as "FCTR".

The novel FCTR nucleic acids of the invention include the nucleic acids whose sequences are provided in Tables 1A, 2A, 3A, 3C, 3E, 3F, 3G, 3H, 4A, 5A, 5C, 5E, 6A, 6C,

and 7A inclusive ("Tables 1A - 7A"), or a fragment, derivative, analog or homolog thereof. The novel FCTR1 proteins of the invention include the protein fragments whose sequences are provided in Tables 1B, 2B, 3B, 3I, 4B, 5B, 5D, 6B, 6D, and 7B inclusive ("Tables 1B - 7B"). The individual FCTR1 nucleic acids and proteins are described below. Within the scope of this invention is a method of using these nucleic acids and peptides in the treatment or prevention of a disorder related to cell signaling or metabolic pathway modulation.

FCTR1

Novel FCTR1 is a growth factor ("FCTR") protein related to follistatin-like gene, and mac25. FCTR1 (also referred to by proprietary accession number 58092213.0.36) is a full-length clone of 771 nucleotides, including the entire coding sequence of a 105 amino acid protein from nucleotides 438 to 753. The clone was originally obtained from thyroid gland, kidney, fetal kidney, and spleen tissues.

The nucleotide sequence of FCTR1 as presently determined is reported in Table 1A. The start and stop codons are bolded and the 5' and 3' untranslated regions are underlined.

Table 1A. FCTR1 nucleotide sequence (SEQ ID NO:1).

GGTCCTCACCCCTTCTCTCTCCAGCCTCGGTGTCTGGTTACGGCTCCTCTGCTCGCATTTGTGACTTTGGGCCAGGCTGGG
GGAAATGACCCGGGAGGGTCCCATGCGGCTACATAAAATTGGCAGCCTTAGAACTAGTGGGAAGGCGGGTGCGCGAAGTCGAG
GGGCGGAGAGAGGGGGCCGGAGGAGTGCTTTCTGAATCCAAGTTCGTGGGCTCTCTCAGAAGTCCTCAGGACGGAGCAGAGG
TGGCCGGCGGGCCCGGCTGACTGCGCCTCTGCTTTCTTCCATAACCTTTCTTTTCGGACTCGAATCACGGCTGCTGCGAAGG
GTCTAGTTCGGACACTAGGGCCCCAGATCGTGTACATCCATATGACACTTGGAAATGTGACAGGGCAGGATGTGATCTTTGG
CTGTGAAGTGTTCCTACCCATGGCCTCCATCGAGTGGAGGAAGGATGGCTTGGACATCCAGCTGCCAGGGGATGACCCCC
ACATCTCTGTGCACTTTAGGGGTGGACCCAGAGGTTTGAAGTGACTGGCTGGCTGCAGATCCAGGCTGTGCGTCCCAAGTGAT
GAGGGCACTTACCGCTGCCTTGCCCGCAATGCCCTGGGTCAAGTGGAGGCCCTGCTAGCTTGACAGTGCTCACACCTGACCA
GCTGAACCTACAGGCATCCCCAGCTGCGATCACTAACCTGGTTCCTGAGGAGGAGGCTGAGAGTGAAGAGAATGACGATT
ACTACTAGGTCAGAGCTCTGGCC

The predicted amino acid sequence of FCTR1 protein corresponding to the foregoing nucleotide sequence is reported in Table 1B. FCTR1 was searched against other databases using SignalPep and PSort search protocols. The protein is most likely located in the cytoplasm (certainty=0.6500) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR1 protein is 11711.8 daltons.

Table 1B. Encoded FCTR1 protein sequence (SEQ ID NO:2).

MASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTPDQLNSTGIP
QLRSLNLPVEEEAESEENDYY

FCTR1 was initially identified with a TblastN analysis of a proprietary sequence file for a follistatin-like probe or homolog which was run against the Genomic Daily Files made available by GenBank. A proprietary software program (GenScan™) was used to further

predict the nucleic acid sequence and the selection of exons. The resulting sequences were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length protein.

In an analysis of sequence databases, it was found, for example, that the FCTR1 nucleic acid sequence has 31/71 bases (43%) identical and 46/71 bases positively alike to a *Mus Musculus* IGFBP-like protein (TREMBL Accession Number:BAA21725) shown in Table 1C. In all BLAST alignments herein, the "E-value" or "Expect" value is a numeric indication of the probability that the aligned sequences could have achieved their similarity to the BLAST query sequence by chance alone, within the database that was searched. For example, as shown in Table 1C, the probability that the subject ("Sbjct") retrieved from the FCTR1 BLAST analysis, in this case the *Mus Musculus* IGFBP-like protein, matched the Query FCTR1 sequence purely by chance is 1.2×10^{-11} .

Table 1C. BLASTP of FCTR1 against *Mus Musculus* IGFBP-like protein (SEQ ID NO:38)

PTNR:REMTREMBL-ACC:BAA21725 IGFBP-LIKE PROTEIN - MUS MUSCULUS (MOUSE), 270 AA.
LENGTH = 270

SCORE = 161 (56.7 BITS), EXPECT = 1.2×10^{-11} , P = 1.2×10^{-11}
IDENTITIES = 31/71 (43%), POSITIVES = 46/71 (64%)

QUERY: 9 DGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPAS 68
+||+ +||| +|+| ||| | | + | + | || | | | |+|+ ++ +
SBJCT: 191 EGLE-ELPGDHVNIQVRRGSPDHETTSWILINPLRKEDEGVYHCHAANAIGEAQSHGT 249
QUERY: 69 LTVLTPDQLNS 79
+||| ++ |
SBJCT: 250 VTVLDLNRYS 260

The amino acid sequence of FCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus Musculus* Follistatin-like Protein shown in Table 1D.

Table 1D. BLASTP of FCTR1 against *Mus Musculus* Follistatin-like Protein (SEQ ID NO:39)

PTNR:SPTREMBL-ACC:Q61581 FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN) - MUS MUSCULUS (MOUSE), 238 AA.
LENGTH = 238

SCORE = 149 (52.5 BITS), EXPECT = 1.5×10^{-10} , P = 1.5×10^{-10}
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
||| +++++ ||||++ |||||+ + + | | | | | + | | | +||+

SBJCT: 165 LPGDRENLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGGASAAAKITVV 222

The amino acid sequence of FCCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* MAC25 protein shown in Table 1E.

Table 1E. BLASTP of FCCTR1 against *Homo sapiens* MAC25 protein (SEQ ID NO:40)

PTNR:SPTREMBL-ACC:Q07822 MAC25 PROTEIN - HOMO SAPIENS (HUMAN), 277 AA.
LENGTH = 277

SCORE = 149 (52.5 BITS), EXPECT = 3.2E-10, P = 3.2E-10
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
|||| +++++| ||||++ |||||+ + + | | | | | + | | | + || +
SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGGASASAKITVV 266

The amino acid sequence of FCCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Mus musculus* MAC25 protein shown in Table 1F.

Table 1F. BLASTP of FCCTR1 against *Mus musculus* MAC25 protein (SEQ ID NO:41)

PTNR:SPTREMBL-ACC:O88812 MAC25 - MUS MUSCULUS (MOUSE), 281 AA
LENGTH = 281

SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
|||| +++++| ||||++ |||||+ + + | | | | | + | | | + || +
SBJCT: 208 LPGDRENLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGGASAAAKITVV 265

The amino acid sequence of FCCTR1 also had 26/58 bases (44%) identical, and 38/58 bases (65%) positive for *Homo sapiens* Prostacyclin-stimulating factor shown in Table 1G.

Table 1G. BLASTP of FCCTR1 against *Homo sapiens* Prostacyclin-stimulating factor (SEQ ID NO:42)

PTNR:SPTREMBL-ACC:Q16270 PROSTACYCLIN-STIMULATING FACTOR - HOMO SAPIENS (HUMAN), 282 AA
LENGTH = 282

SCORE = 149 (52.5 BITS), EXPECT = 3.4E-10, P = 3.4E-10
IDENTITIES = 26/58 (44%), POSITIVES = 38/58 (65%)

QUERY: 15 LPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALGQVEAPASLTVL 72
|||| +++++| ||||++ |||||+ + + | | | | | + | | | + || +
SBJCT: 209 LPGDRDNLAIQTRGGPEKHEVTGWVLVSPLSKEDAGEYECHASNSQGGASASAKITVV 266

The amino acid sequence of FCCTR1 also had 18/44 bases (40%) identical, and 25/44 bases (56%) positive for rat Colorectal cancer suppressor shown in Table 1H.

Table 1H. BLASTP of FCCTR1 against rat Colorectal cancer suppressor (SEQ ID NO:43)

PTNR:PIR-ID:B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS)
LENGTH = 144

SCORE = 78 (27.5 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
IDENTITIES = 18/44 (40%), POSITIVES = 25/44 (56%)

QUERY: 33 FEVTGW--LQIQAVRPSDEGTYRCLARNALGQVEAPASLTVLTP 74
|++ | | + | | ||| | + | + | | ++ | | |
SBJCT: 101 FQIVGGSNLRILGVVKSDEGFYQCVAENEAGNAQSSAQLIVPKP 144

SCORE = 37 (13.0 BITS), EXPECT = 1.1E-05, SUM P(2) = 1.1E-05
IDENTITIES = 8/19 (42%), POSITIVES = 12/19 (63%)

QUERY: 1 MASIEWRKDGLDIQL-PGD 18
| + | | + | + | + | | |
SBJCT: 30 MPTIHWQKNQQDLTPNPGD 48

The amino acid sequence of FCCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive to bases 55-137, and 24/68 bases (35%) identical, and 37/68 bases (54%) positive to bases 166-225 of *Homo sapiens* PTPsigma-(Brain) Precursor shown in Table II.

Table 1I. BLASTP of FCCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:44)

PTNR:TREMBLNEW-ACC:AAD09360 PTPSIGMA-(BRAIN) PRECURSOR - HOMO SAPIENS (HUMAN), 1502 AA.
LENGTH = 1502

SCORE = 109 (38.4 BITS), EXPECT = 0.00010, P = 0.00010
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

QUERY: 14 QLPGDD-PHISVQFRG---GPQRFVETGW-----LQIQAVR-PSDEGTYRCLARNALG 61
| | | | + + + | | | | + | | | + | | | + | + | + |
SBJCT: 55 QATGDPKPRVTWNKKGKVNQSRFETIEFDESAGAVLRILQPLRTPRDENVYECVAQNSVG 114

QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85
++ | | | | | | | | +
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

SCORE = 77 (27.1 BITS), EXPECT = 0.25, P = 0.22
IDENTITIES = 24/68 (35%), POSITIVES = 37/68 (54%)

QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFVETGWLQIQAVRPSDEGTYRCLARNALG-Q 62
| | | | + | | | | + + + | | | + + | + | | + | + | +
SBJCT: 166 ITWFKDFLPV-----DPSAS---NGRIKQLR-SGALQIESSEETDQGKYECVATNSAGVR 216

QUERY: 63 VEAPASLTV 71
+ | + | |
SBJCT: 217 YSSPANLYV 225

The amino acid sequence of FCCTR1 also had 32/83 bases (38%) identical, and 45/83 bases (54%) positive for amino acids 55-137 and 26/69 bases (37%) identical, and 38/69

(54%) positive for amino acids 166-234 of *Homo sapiens* Protein-Tyrosine Phosphatase
Sigma shown in Table 1J.

Table 1J. BLASTP of FCTR1 against *Homo sapiens* PTPsigma-(Brain) Precursor (SEQ ID NO:45)

5 PTNR:SPTREMBL-ACC:Q13332 PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, S PRECURSOR
(EC 3.1.3.48) (PROTEIN-TYROSINE PHOSPHATASE SIGMA) (R-PTP-SIGMA) (PTPRS) - HOMO
SAPIENS (HUMAN), 1948 AA.
LENGTH = 1948

10 SCORE = 109 (38.4 BITS), EXPECT = 0.00013, P = 0.00013
IDENTITIES = 32/83 (38%), POSITIVES = 45/83 (54%)

15 QUERY: 14 QLPGDD-PHISVQFRG---GPQRFEVTGW-----LQIQAVR-PSDEGTYRCLARNALG 61
| | | | ++ + | | | | + | + | | | | | + | + | + |
SBJCT: 55 QATGDPKPRVTWNKKGKKVNSQRFETIEFDESAGAVLR IQPLRTPRDENVYECVAQNSVG 114

20 QUERY: 62 QVEAPASLTVLTPDQLNSTGIPQL 85
++ | | | | | | | | +
SBJCT: 115 EITVHAKLTVLREDQLPS-GFPNI 137

25 SCORE = 88 (31.0 BITS), EXPECT = 0.023, P = 0.022
IDENTITIES = 26/69 (37%), POSITIVES = 38/69 (55%)

30 QUERY: 4 IEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVT---GWLQIQAVRPSDEGTYRCLARNAL 60
| | | | + + | | | + | | | | | | ++ + | + | | + | +
SBJCT: 166 ITWFKDFLPVDPSPASNGRIK-QLRS--ETFEPTPIRGALQIESSEETDQGKYECVATNSA 222

35 QUERY: 61 G-QVEAPASLTV 71
| + + | + | |
SBJCT: 223 GVRYSSPANLYV 234

A ClustalW analysis comparing the protein of the invention with related protein sequences is given in Table 1K, with FCTR1 shown on line 2. In the ClustalW alignment of the FCTR1 protein, as well as all other ClustalW analyses herein, the black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties), whereas non-highlighted amino acid residues are less conserved and can potentially be mutated to a much broader extent without altering protein structure or function.

Table 1K. ClustalW Analysis of FCTR1

40 1) Q07822 MAC25 PROTEIN. (SEQ ID NO:40)
2) Q16270 PROSTACYCLIN-STIMULATING FACTOR. (SEQ ID NO:42)
3) Q61581 FOLLISTATIN-LIKE 2: FOLLISTATIN-LIKE 2 (FOLLISTATIN-LIKE PROTEIN)
(SEQ ID NO:39)

45 4) BAA21725 IGFBP-LIKE PROTEIN (SEQ ID NO:38)
5) FCTR1 (SEQ ID NO:2)
6) B40098 COLORECTAL CANCER SUPPRESSOR DCC - RAT (FRAGMENTS) (SEQ ID NO:43)

50 Q07822 MERASLRALLFGPAGLLLLLLPLSSSSSSDTCCGPCEPASCPPLPPLGCLLGETRDACGCC
Q16270 MERPSLRALLGAAGLLLLLLPLSSSSSSDTCCGPCEPASCPPLPPLGCLLGETRDACGCC
Q61581 MERP PRALLLGAAGLLLLLLPLSSSSSSDACGR
BAA21725 MPRLP LLLLLPSLARGLGLRDAG RRHPECSPCQQDRCPAPSPCPAPWISAREDCGCC
FCTR1

B40098

Q07822 PMCARGECEPCGGGAGRCYCAPGMECVKSRKRRRGKAGAAAGGPVSGVCVCKSRYPVC
Q16270 PMCARGECEPCGGGAGRCYCAPGMECVKSRKRRRGKAGAAAGGPVSGVCVCKSRYPVC
5 Q61581_ RCHCAPGMECVKSRKRRRGKAGAAAGGPATLAVCVCKSRYPVC
BAA21725 ARCLGAEAGASCG CPVGSRCSPGLVCA SR ASCTPEEC T GECVGAQRGAVC
FCTR1
B40098 PPRFLSQTESIT

10 Q07822 GSDGTTYPSCGQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV
Q16270 GSDGTTYPSCGQLRAASQRAESRGEKA ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV
Q61581_ GSNCTITYPSCGQLRAASLRAESRGEKP ITQVSKGTCEQGPSIVTPPKDIWNVTGAQV
BAA21725 GSDGRSYSSITCALRLRARHAPRAHHGH HKARDGCPCEFAFVVMPPRDIFNVVTGTOV
FCTR1

15 B40098 AFMCDITVLLKCEVIIDPMPTIHWQKNQDLTPNPGDSRVVVPFWFENHPSNLYAYESMDI

20 Q07822 YLSCEVIGIPTPVLINWVKRGHYGVQRTPELLPGDRNLAIQTRGGPEKHEVTGWVLVSP
Q16270 YLSCEVIGIPTPVLINWVKRGHYGVQRTPELLPGDRNLAIQTRGGPEKHEVTGWVLVSP
Q61581_ YLSCEVIGIPTPVLINWVKRGHSGVQRTPELLPGDRNLAIQTRGGPEKHEVTGWVLVSP
BAA21725 YLSCEVKAMPTPVITWKKVKHSPECTEGLEELPGDHVNIAWQVRGGSDEHETTSWILLNE
FCTR1 MASTENRKDGLDIO.....LPGDPHLSVQFRGGPQRFVETGWLQIQQA
B40098 EFECVAVSCKEVETVNMKNGDVVV.....ISDYFCIVGGSN.....ERLLG

25 Q07822 LSKEDAGEYECHASNSQGQASASAKITVVDALHEIAS.....EKR....
Q16270 LSKEDAGEYECHASNSQGQASASAKITVVDALHEIPV.....KKGEGAE
Q61581_ LSKEDAGEYECHASNSQGQASAAAKITVVDALHEIPV.....KKGEGAQ
BAA21725 LRKEDGCVYHCHAANATCEAQSHGTITVVDLNLRYKSL.....YSSVPGD
FCTR1 VRPSDECTVRCILARNALCOVEAPSLITVETPDQLNSTGIPQLRSLNLVPEEEAESEEND
B40098 VVKSDGEGFVQCVAEENEACNAQSSAOLIVPKP.....

30 Q07822
Q16270
Q61581_
BAA21725
35 FCTR1
YY

IGFBP is expressed in neurostem cell and developing central nervous system. MAC-25, a follistatin like protein is a growth suppressor of osteosarcoma cells, and meningiomas. DCC is expressed in most normal tissues especially in colonic mucosa, but is deleted in colorectal cancers.

Since FCTR1 has similarity to these proteins (shown in BlastP, Tables 1C-1J, and in clustalW, Table 1K) it is likely that it has similar function. Therefore FCTR1 could function as on or more of the following: a tumor suppressor gene or regulator of neurological system development.

Based on the protein similarity and tissue expression, FCTR1 may be useful in the following diseases and uses:

- (i) Tissue regeneration in vitro and in vivo
- (ii) Neurological disorders, neurodegenerative disorders, nerve trauma
- (iii) Reproductive health
- (iv) Immunological disorders, allergy and infection
- (v) In cancer as a diagnostic and prognostic marker, as well as a protein therapeutic

FCTR2

FCTR2 (alternatively referred to herein as AC012614_1.0.123), is a growth factor bearing sequence similarity to human KIAA1061 protein and to genes involved in neuronal development and reproductive physiology (e.g., cell adhesion molecules, follistatin, roundabout and frazzled). FCTR2 is a full-length clone of 5502 nucleotides, including the entire coding sequence of a 815 amino acid protein. This sequence is expressed in glioma, osteoblast, other cancer cells, lung carcinoma, small intestine (This sequence maps to Unigene Hs.123420 which is expressed in brain, breast, kidney, pancreas, pooled tissue).

A FCTR2 ORF begins with an ATG initiation codon at nucleotides 420-422 and ends with a TGA codon at nucleotides 2865-2867. Putative untranslated regions upstream from the initiation codon and downstream from the termination codon are underlined in Table 2A, and the start and stop codons are in bold letters.

Table 2A. FCTR2 Nucleotide Sequence (SEQ ID NO:3).

CAATTTACACAGGAAACAGCTATGCCATGATTACGCAAGTTGGTACCGAGCTCGGATCCACTAGTAACGGCCGCCAGTG
TGCTGGAATTCGGCTTACTCACTATAGGGCTCGAGCGGCTGCCCGGGCAGGTCATTAAATCCATTTCTTTTAGAGTATC
ACAGCTTTCTCCTTCACTGACCACCCTTTGCTTCTGTGTCAGAAAGCCCTGGACAGAACTCTGTGGGATTCTGCCCATG
TTTCTGAGATATCGCCTCAATTGTCTGGCTGGGCTGTGGGCTGTGCCGTTTTACAGATGGGCAAACTGGAGTGGGAAG
TATCCGGGTGGCTTCTCAGGCTGTCAGCTGGTGGAGCAGCTACTGAAACAATCAGGAGCCAGAACTTTGAAGTCACA
AGAAGAGAAGACTCCAGAAATGCAGTGTGATGTTGGTATGGACGCTGTTTCGCCTTTCACTTAAACGTGCCCTTTCCA
GCTGCCCTGACCTCTTTGGGCTTTCCAGCCGCAACGAGCTGCTGGCCTCTGCGGGAAGAAGTTCTGCAGCCGAGGGAGC
CGGTGCGTGCTCAGCAGGAAGACAGGGGAGCCGAATGCCAGTGCTGGAGGCATGCAGGCCAGCTACGTGCCCTGTGTG
CGGCTCTGATGGGAGGTTTTATGAAACCACCTGTAAGCTCCACGCTGCTGCTTGCCTCCTGGGAAAGAGGATCACCGTCA
TCCACAGCAAGGACTGTTTCTCAAAGGTGACACGTGACCATTGGCCGGCTACGCCGCTTGAAGAATGCTCTTCTGGCA
CTCCAGACCCTGTCAGCCACTCCAAGAAGGAGACAGACAGCAAGACCCTGCCTCCAGAAAGCGCCTCTGGTGGGAATC
TCTGTTACAGGACTTAGATGCAGATGGCAATGGCCACCTCAGCAGCTCCGAAGTGGCTCAGCATGTGCTGAAGAAGCAGG
ACCTGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCGATTGACGATTACAACAGTGACAGCTCCTTGACC
CTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTCAGCTCAGCCTCGCCCCGAGGACAGGGTCAGTGTGACCACAGTGAC
CGTGGGGCTGAGCACAGTGTGACCTGCGCGTCCATGGAGACTGAGGCCACCAATCATCTGGAAGCGCAACGGGCTCA
CCTGAACCTTCTTGACTTGGAAAGACATCAATGACTTTGGAGAGGATGATTCCTGTACATCACCAAGGTGACCACCATC
CACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGCTGTTCCAGACCCAGCTCCTGCAGGTGAATGTGCCGCC
AGTCATCCGTGTCTATCCAGAGAGCCAGGCACAGGAGCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATT
CCATGCCCAGAAATCACTTGGCTGAAAACCGCGTGGATGCTCAACTCAGATGTCCAAACAGCTCTCCCTTTAGCCAAT
GGGAGCGAACTCCACATCAGCAGTGTTCGGTATGAAGACACAGGGGCATACACCTGCATTGCCAAAATGAAGTGGGTGT
TGATGAAGATATCTCCTCGCTCTTCAATTGAAGACTCAGCTAGAAAGACCCTTGCAACATCCTGTGGCGAGAGGAAGGCC
TCAGCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTATCCATCCTGTGGACTGTGAGATCCAGAGG
CACCTCAAACCCACGGAAGATTTTATGAGCTATGAAGAAATCTGTCTCAAAGAGAAAAAATGCAACCCAGCCCTG
CCAGTGGGTATCTGCAGTCAATGTCCGGAACCGGTACATCTATGTGGCCAGCCAGCACTGAGCAGAGTCTTGTGGTGC
ACATCCAAGCCAGAAAGTCTACAGTCCATAGGTGTGGACCCTCTGCCGCTAAGCTGTCTATGACAAGTCACATGAC
CAAGTGTGGTCTCTGAGCTGGGGGACGTGCACAAGTCCCGACCAAGTCTCCAGGTGATCAGAGAAGCCAGCACCGCCA
GAGCCAGCACCTCATCCGCACACCCTTTGAGGAGTGGATGATTTCTTATTCCCCCAACAAACCTCATCATCAACCACA
TCAGGTTTGGCTTCTTCAACAAGTCTGATCTGCAGTCCACAAGGTGGACCTGGAAACAATGATGCCCTCAAGACC
ATCGGCTGCACCACCATGGCTGCGTGCCCGAGCCATGGCACACACCACCTGGGCGGCTACTTCTTATCCAGTGCCG
ACAGGACAGCCCCGCTCTGCTGCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCAATGGTGATG
TAACAGGCACCCACACACATCCCCGACGGGCTTCCATAGTCAAGTGTGCTGAGCTGACAGCCCTGGCTGACGTGCAG
GAGATCACAGTGCAGGGCGAGATCCAGACCCTGTATGACCTGCAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCG
CTCCTTCACTGAAAGCAATCAATACAACATCTACGCGGCTGTGCACACGAGCCGACCTGCTGTTCTGGAGCTGTCCA
CGGGGAAGTGGGCTGCTGAGAATTAAGAGGACCCCGCAGGGCCAGCTCAGCCTGGGGGGTATCCACAGAATC
ATGAGGGACAGTGGGCTGTTTGGACAGTACCTCTCACACCAGCCGAGAGTCACTGTTCTCATCAATGGGAGACAAA
ACGCTGCGGTGTGAGGTATGAGGTATAAAGGGGGGACACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCA
GAGCCTGGGCCAAGGAACACCCCTAGTCTGACACTGCAGCCTCAAGCAGGTACGCTGTACATTTTACAGACAAAAG
CAAAAACCTGTACTCGCTTTTGGTTCAACACTGGTCTCCTTGCAAGTTTCTAGTATAAGGTATGCGCTGTACCAAGA
TTGGGGTTTTTCTGTTAGGAAGTATGATTTATGCCTTGAGTACGATGAGAACATATGCTGTGTGTAAGGGATCATTT
CTGTGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCAAGCAGACACCTCTGTCA

Table 2C. BLASTN of FCTR2 against *Homo sapiens* mRNA for KIAA1061 protein
(SEQ ID NO:46)

>GI|5689458|DBJ|AB028984.1|AB028984 HOMO SAPIENS MRNA FOR KIAA1061 PROTEIN, PARTIAL
 CDS

5 LENGTH = 4719

SCORE = 9075 BITS (4578), EXPECT = 0.0

IDENTITIES = 4672/4719 (99%)

STRAND = PLUS / PLUS

10

QUERY: 784 AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 843
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1 AGAATGTCCTTCTGGCACTCCAGACCCGTCTGCAGCCACTCCAAGAAGGAGACAGCAGAC 60

15

QUERY: 844 AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGAATCTCTGTTTCAGGGACTTAGATGCAG 903
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 61 AAGACCCTGCCTCCCAGAAGCGCCTCCTGGTGAATCTCTGTTTCAGGGACTTAGATGCAG 120

20

QUERY: 904 ATGGCAATGGCCACCTCAGCAGCTCCGAAGTGGCTCAGCATGTGCTGAAGAAGCAGGACC 963
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 121 ATGGCAATGGCCACCTCAGCAGCTCCGAAGTGGCTCAGCATGTGCTGAAGAAGCAGGACC 180

25

QUERY: 964 TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTGACGATTACAACA 1023
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 181 TGGATGAAGACTTACTTGGTTGCTCACCAGGTGACCTCCTCCGATTGACGATTACAACA 240

30

QUERY: 1024 GTGACAGCTCCCTGACCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTTCAGCTCAGCC 1083
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 241 GTGACAGCTCCCTGACCTCCGCGAGTTCTACATGGCCTTCCAAGTGGTTTCAGCTCAGCC 300

35

QUERY: 1084 TCGCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 1143
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 301 TCGCCCCGAGGACAGGGTCAGTGTGACCACAGTGACCGTGGGGCTGAGCACAGTGCTGA 360

40

QUERY: 1144 CCTGCGCCGTCCTGAGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGGCTACCC 1203
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 361 CCTGCGCCGTCCTGAGAGACCTGAGGCCACCAATCATCTGGAAGCGCAACGGGGCTACCC 420

45

QUERY: 1204 TGAACCTCCTGGACTTGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 1263
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 421 TGAACCTCCTGGACTTGAAGACATCAATGACTTTGGAGAGGATGATTCCCTGTACATCA 480

50

QUERY: 1264 CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 1323
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 481 CCAAGGTGACCACCATCCACATGGGCAATTACACCTGCCATGCTTCCGGCCACGAGCAGC 540

55

QUERY: 1324 TGTTCAGACCCACGTCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 1383
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 541 TGTTCAGACCCACGTCTGCAGGTGAATGTGCCGCCAGTCATCCGTGTCTATCCAGAGA 600

60

QUERY: 1384 GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 1443
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 601 GCCAGGCACAGGAGCCTGGAGTGGCAGCCAGCCTAAGATGCCATGCTGAGGGCATTCCCA 660

65

QUERY: 1444 TGCCCAAGATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 1503
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 661 TGCCCAAGATCACTTGGCTGAAAAACGGCGTGGATGTCTCAACTCAGATGTCCAAACAGC 720

QUERY: 1504 TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTTCGGTATGAAGACACAG 1563
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 721 TCTCCCTTTTAGCCAATGGGAGCGAACTCCACATCAGCAGTGTTTCGGTATGAAGACACAG 780

QUERY: 1564 GGGCATAACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 1623
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 781 GGGCATAACCTGCATTGCCAAAAATGAAGTGGGTGTGGATGAAGATATCTCCTCGCTCT 840

TABLE "B6T00860"

QUERY: 1624 TCATTGAAGACTCAGCTAGAAAGACCCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 1683
 SBJCT: 841 TCATTGAAGACTCAGCTAGAAAGACCCCTTGCAAACATCCTGTGGCGAGAGGAAGGCCTCA 900
 5
 QUERY: 1684 GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 1743
 SBJCT: 901 GCGTGGGAAACATGTTCTATGTCTTCTCCGACGACGGTATCATCGTCATCCATCCTGTGG 960
 10
 QUERY: 1744 ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAGATTTTCATGAGCTATGAAGAAA 1803
 SBJCT: 961 ACTGTGAGATCCAGAGGCACCTCAAACCCACGGAAGATTTTCATGAGCTATGAAGAAA 1020
 QUERY: 1804 TCTGTCTCTCAAAGAGNNNNNNNTGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1863
 SBJCT: 1021 TCTGTCTCTCAAAGAGAAAAAATGCAACCCAGCCCTGCCAGTGGGTATCTGCAGTCAATG 1080
 15
 QUERY: 1864 TCCGGAACCGGTACATCTATGTGGCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCGACA 1923
 SBJCT: 1081 TCCGGAACCGGTACATCTATGTGGCCAGCCAGCACTGAGCAGAGTCCTTGTGGTCGACA 1140
 20
 QUERY: 1924 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1983
 SBJCT: 1141 TCCAAGCCCAGAAAGTCCTACAGTCCATAGGTGTGGACCCTCTGCCGGCTAAGCTGTCCT 1200
 25
 QUERY: 1984 ATGACAAGTCACATGACCAAGTGTGGGTCTGAGCTGGGGGACGTGCACAAGTCCCGAC 2043
 SBJCT: 1201 ATGACAAGTCACATGACCAAGTGTGGGTCTGAGCTGGGGGACGTGCACAAGTCCCGAC 1260
 30
 QUERY: 2044 CAAGTCTCCAGGTGATCAGAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 2103
 SBJCT: 1261 CAAGTCTCCAGGTGATCAGAGAAGCCAGCACCGGCCAGAGCCAGCACCTCATCCGCACAC 1320
 QUERY: 2104 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 2163
 SBJCT: 1321 CCTTTGCAGGAGTGGATGATTTCTTCATTCCCCCAACAAACCTCATCATCAACCACATCA 1380
 35
 QUERY: 2164 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 2223
 SBJCT: 1381 GGTTTGGCTTCATCTTCAACAAGTCTGATCCTGCAGTCCACAAGGTGGACCTGGAAACAA 1440
 40
 QUERY: 2224 TGATGCCCCCTCAAGACCATCGGCCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 2283
 SBJCT: 1441 TGATGCCCCCTCAAGACCATCGGCCCTGCACCACCATGGCTGCGTGCCCCAGGCCATGGCAC 1500
 45
 QUERY: 2284 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCTCTGCTG 2343
 SBJCT: 1501 ACACCCACCTGGGCGGCTACTTCTTCATCCAGTGCCGACAGGACAGCCCCGCTCTGCTG 1560
 50
 QUERY: 2344 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 2403
 SBJCT: 1561 CCCGACAGCTGCTCGTTGACAGTGTACAGACTCTGTGCTTGGCCCCAATGGTGATGTAA 1620
 QUERY: 2404 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 2463
 SBJCT: 1621 CAGGCACCCACACACATCCCCGACGGGCGCTTCATAGTCAGTGCTGCAGCTGACAGCC 1680
 55
 QUERY: 2464 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 2523
 SBJCT: 1681 CCTGGCTGCACGTGCAGGAGATCACAGTGCGGGGCGAGATCCAGACCCTGTATGACCTGC 1740
 60
 QUERY: 2524 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 2583
 SBJCT: 1741 AAATAAACTCGGGCATCTCAGACTTGGCCTTCCAGCGCTCCTTCACTGAAAGCAATCAAT 1800
 65
 QUERY: 2584 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTGGAGCTGTCCACGG 2643
 SBJCT: 1801 ACAACATCTACGCGGCTCTGCACACGGAGCCGGACCTGCTGTTCTGGAGCTGTCCACGG 1860

QUERY: 2644 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTNNN 2703
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1861 GGAAGGTGGGCATGCTGAAGAACTTAAAGGAGCCACCCGAGGGCCAGCTCAGCCCTGGG 1920

 5 QUERY: 2704 NNNNTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 2763
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1921 GGGGTACCCACAGAATCATGAGGGACAGTGGGCTGTTTGGACAGTACCTCCTCACACCAG 1980

 10 QUERY: 2764 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCTAG 2823
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1981 CCCGAGAGTCACTGTTCTCATCAATGGGAGACAAAACACGCTGCGGTGTGAGGTGTCTAG 2040

 QUERY: 2824 GTATAAANNNNNNNACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCAGAG 2883
 ||||||| ||||||||||||||||||||||||||||||||||||||||||||||||
 15 SBJCT: 2041 GTATAAAGGGGGGACCACAGTGGTGTGGGTGGGTGAGGTATGAAGGGCCAGAGCAGAG 2100

 QUERY: 2884 CCCTGGGCCAAGGAACACCCCTAGTCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2943
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 20 SBJCT: 2101 CCCTGGGCCAAGGAACACCCCTAGTCTGACACTGCAGCCTCAAGCAGGTACGCTGTAC 2160

 QUERY: 2944 ATTTTACAGACAAAAGCAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCTCTTG 3003
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2161 ATTTTACAGACAAAAGCAAAACCTGTACTCGCTTTGTGGTTCAACACTGGTCTCTCTTG 2220

 25 QUERY: 3004 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 3063
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2221 CAAGTTTCCTAGTATAAGGTATGCGCTGCTACCAAGATTGGGGTTTTTTCGTTAGGAAGT 2280

 QUERY: 3064 ATGATTATGCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTCTCTG 3123
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 30 SBJCT: 2281 ATGATTATGCTTGAGCTACGATGAGAACATATGCTGCTGTGTAAAGGGATCATTCTCTG 2340

 QUERY: 3124 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 3183
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 35 SBJCT: 2341 TGCCAAGCTGCACACCGAGTGACCTGGGGACATCATGGAACCAAGGGATCCTGCTCTCCA 2400

 QUERY: 3184 AGCAGACACCTCTGTGAGTTGCCTTACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 3243
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 40 SBJCT: 2401 AGCAGACACCTCTGTGAGTTGCCTTACATAGTCATTGTCCCTTACTGCCAGACCCAGCC 2460

 QUERY: 3244 AGACTTTGCCCTGACGGAGTGGCCCGAAGCAGAGGCGGACCAGGAGCAGGGGCCTCCCT 3303
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2461 AGACTTTGCCCTGACGGAGTGGCCCGAAGCAGAGGCGGACCAGGAGCAGGGGCCTCCCT 2520

 45 QUERY: 3304 CCCGAACTGAAAGCCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 3363
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2521 CCCGAACTGAAAGCCCATCCGTCTCGCGTGGGACCGCATCTTCTCCCTCGCAGCTGCTT 2580

 QUERY: 3364 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAAGCCTGAGGGAGAGCCAACAAGACTTACTG 3423
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 50 SBJCT: 2581 CTTGCTTTTCTTTCCATTTGACTTGCTGTAAAGCCTGAGGGAGAGCCAACAAGACTTACTG 2640

 QUERY: 3424 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGAAATTTTGATTNNNNNNNNNT 3483
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 55 SBJCT: 2641 CATCTTGGGGGATGGGGAAATCACTCACTTTATTTTGAAATTTTGATTAAAAAAAAT 2700

 QUERY: 3484 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAATATATCCTTC 3543
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 60 SBJCT: 2701 TTTATAATCTCAAATGCTAGTAAGCAGAAAGATGCTCTCCGAGGTCCAATATATCCTTC 2760

 QUERY: 3544 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCAACAACCCACATCCACAGCCAGAAAGAAC 3603
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2761 CCTGCCTTAGGCCGAGTCTCGGGGGTGGTCAACAACCCACATCCACAGCCAGAAAGAAC 2820

 65 QUERY: 3604 AATGGTCATCTGAGAATACTGGCCCTGTGACTATTGCCACCCTGCTTCTCCAAGAGCAG 3663
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2821 AATGGTCATCTGAGAATACTGGCCCTGTGACTATTGCCACCCTGCTTCTCCAAGAGCAG 2880

QUERY: 3664 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAACCAGAACA 3723
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2881 ACCAGGCCACCTCATCCGTAAGGACTCGGTTCTGTGTTGGGACCCCAAAAACCAGAACA 2940
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

5 QUERY: 3724 AGTTCTGTGTGCCTCCTTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3783
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2941 AGTTCTGTGTGCCTCCTTTTCAGCACAGAAGGGAGACATCTCATTAGTCAGGTCTGGTACC 3000
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

10 QUERY: 3784 CCAGATTTCAGGGCAGACTGGGCTTGCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3843
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3001 CCAGATTTCAGGGCAGACTGGGCTTGCTGGCAAGGTATGGGTGGCCTCCAGGCTCAATGC 3060
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

15 QUERY: 3844 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAC 3903
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3061 AGAAACCCCAAGGACACGAGTGGGGCCAGGTGAGTTCCTGAAGCTATACCTTTTCAAAC 3120
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

20 QUERY: 3904 AGATTTTGTCTTCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3963
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3121 AGATTTTGTCTTCTACCTGTGGCCCATCCACTCCTCTCTGGTACCCCATCCCCGCATCA 3180
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

25 QUERY: 3964 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTCTTACCCACATTCCCAATCAATAC 4023
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3181 GCACTGCAGAGAGAACACATTTTCGGCGAGGGTTTCTTACCCACATTCCCAATCAATAC 3240
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

30 QUERY: 4024 ACACACACTGCAGAACCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 4083
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3241 ACACACACTGCAGAACCAGAACAGAAGGCCACAGGCTGGCACTACTGCATTCTCCTTAT 3300
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

35 QUERY: 4084 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCACATAGCCCT 4143
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3301 GTGTCTCAGGCTGTGGTGACTCTCACATGGGCATCGAAGAAGTACAACCACATAGCCCT 3360
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

40 QUERY: 4144 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 4203
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3361 CTGGAGACCGCCTAGATCAGAGACTCAGCAAAAACAGGCTCGCCTTCCCTCTCCACATA 3420
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

45 QUERY: 4204 TGAGTGGAACCTTACATGTGTCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 4263
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3421 TGAGTGGAACCTTACATGTGTCTGGTTTGAATGATCATTTTGCAAGCCACACGGGTGGG 3480
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

50 QUERY: 4264 AGAGGTGGTCTCACCACAGCGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 4323
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3481 AGAGGTGGTCTCACCACAGCGTCTTTGCTAATTTGGCCACCTTCACCTACTGACATGAC 3540
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

55 QUERY: 4324 CAGGATTTTCTTTGCCATTAAGGAATGAACCTTTTCAAGGAGAGGAAACCCTAGACTCT 4383
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3541 CAGGATTTTCTTTGCCATTAAGGAATGAACCTTTTCAAGGAGAGGAAACCCTAGACTCT 3600
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

60 QUERY: 4384 GTGTCACTCTCAACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 4443
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3601 GTGTCACTCTCAACACACAGCTCCTTTCACTCCTGCCTGACTGCCAAGCCACCTGCAT 3660
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

65 QUERY: 4444 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 4503
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3661 CCCCCGCCCCAGATCTCATGAGATCAATCACTTGTATGTCTCACGCAACTTGGTCCACCA 3720
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

70 QUERY: 4504 AACGCCTGTCCCCTGTAACCTCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 4563
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3721 AACGCCTGTCCCCTGTAACCTCTAGGGGTGCGCCTAGACAGGTACGTCTGTTTTTTATTT 3780
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

75 QUERY: 4564 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAGCCTAGAATGCAG 4623
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3781 TAAAAGATATGCTATGTAGATATAAGTTGAGGAAGCTCACCTCAAAGCCTAGAATGCAG 3840
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

80 QUERY: 4624 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCNNNNNNNNCCTGCCTCAA 4683
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 3841 TTTCACAGTAGCTGGGATGCATGGATGACCCATCTCACCCCTTTTTTTTCTGCCTCAA 3900
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||

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QUERY: 4684 TATCTTGATATGTTATGTTTACTCCCAATCTCCCATTTTTTACCACTAAAATTCTCCAAC 4743
          |||
SBJCT: 3901 TATCTTGATATGTTATGTTTACTCCCAATCTCCCATTTTTTACCACTAAAATTCTCCAAC 3960

5  QUERY: 4744 TTCATAAACNNNNNNNGGAAAAATTTCCATTGTATCAGCCCTGACAGAAAAAGGATCT 4803
          |||
SBJCT: 3961 TTCATAAACTTTTTTTGGAAAAATTTCCATTGTATCAGCCCTGACAGAAAAAGGATCT 4020

10  QUERY: 4804 CTGAGCCTAAAGGAGGAAAAGTCCCACTACCAGACCAGAACACGAGCCCTCTGGG 4863
          |||
SBJCT: 4021 CTGAGCCTAAAGGAGGAAAAGTCCCACTACCAGACCAGAACACGAGCCCTCTGGG 4080

15  QUERY: 4864 CAGCAGGATTCTTAAGTCAAAGACCAGTTTGACCCAACTGGCCTTTTAAAATAATCAGG 4923
          |||
SBJCT: 4081 CAGCAGGATTCTTAAGTCAAAGACCAGTTTGACCCAACTGGCCTTTTAAAATAATCAGG 4140

20  QUERY: 4924 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCACTGTCCCTTCCATCTTGAA 4983
          |||
SBJCT: 4141 AGTGACAGAGTCAACTTCTGCAGCACCTGCTTCTCCCCACTGTCCCTTCCATCTTGAA 4200

25  QUERY: 4984 TGTGTCTAAAAAGCATAGCTGCCCTTTGCTGTCTCAGAGTGCATTTCTGGAGACGGC 5043
          |||
SBJCT: 4201 TGTGTCTAAAAAGCATAGCTGCCCTTTGCTGTCTCAGAGTGCATTTCTGGAGACGGC 4260

30  QUERY: 5044 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACGAATCGAAGCAGGCCTGAAGCCT 5103
          |||
SBJCT: 4261 AGGCTTAGGTCTCACTGACAGCATGCCAGACACAACGAATCGAAGCAGGCCTGAAGCCT 4320

35  QUERY: 5104 AGGTCAGGGTTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 5163
          |||
SBJCT: 4321 AGGTCAGGGTTTTCAGGAGTCCAGCCCCAGGAGGCAAAGTCACCAATGCAGGGAGGTAAAT 4380

40  QUERY: 5164 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGAGTCAGGGGTGGGAGGAGAA 5223
          |||
SBJCT: 4381 GCCTTTTGGCAGGAAAACCAATAGAGTTGGTTGGGTGGGAGTCAGGGGTGGGAGGAGAA 4440

45  QUERY: 5224 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCAGCAGA 5283
          |||
SBJCT: 4441 GGAGGAAGAGGAGGAAGGCCAGACTGGCCTGCCCTTTCTCCCATACTTCACCCAGCAGA 4500

50  QUERY: 5284 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCCTC 5343
          |||
SBJCT: 4501 GGTTCATGGGACACAGTTGGAAAGCCACTGGGAGGAAATGCCTCACTACAGGGGGGCCCTC 4560

55  QUERY: 5344 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTACAACTGAT 5403
          |||
SBJCT: 4561 CTGTAGCAAGCCCAGCCGGTAATCCTCCTAATGAACCCACAAGGTCAATTACAACTGAT 4620

60  QUERY: 5404 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAGAATCATCAAGAAAGCTATTTATA 5463
          |||
SBJCT: 4621 ATCTTAGCTATTAAAGAAGTACTGACTTTACCAAAGAATCATCAAGAAAGCTATTTATA 4680

QUERY: 5464 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 5502
          |||
SBJCT: 4681 TAAACCCCTCAGTCATTTTGAAATAAAATTAATTTTAC 4719

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The FCTR2 amino acid sequence has 473 of 810 amino acid residues (58%) identical to, and 616 of 810 residues (76%) positive with, the 850 amino acid residue proteins from *Homo sapiens* KIAA1263 Protein fragment (ptnr: TREMBLNEW-ACC:BAA86577) (SEQ ID NO:47) (Table 2D).

Amino acids 123-815 of FCTR2 also have 693 of 693 amino acid residues (100%) identical to, the 693 amino acid residue protein fragment of KIAA1061 Protein from *Homo sapiens* (ptnr: TREMBLNEW-ACC: BAA83013) (SEQ ID NO:48) (Table 2E).

5 **Table 2E. BLASTP of FCTR2 against KIAA1061 Protein [Fragment] (SEQ ID NO:48)**

ptnr:TREMBLNEW-ACC:BAA83013 KIAA1061 PROTEIN - Homo sapiens (Human),
693 aa (fragment).

Length = 693

Score = 3623 (1275.4 bits), Expect = 0.0, P = 0.0
Identities = 693/693 (100%), Positives = 693/693 (100%)

```

QUERY: 123 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNHGLSSSELAQHVLKKQDL 182
          |||
15  SBJCT: 1 NVLLALQTRLQPLQEGDSRQDPASQKRLLVESLFRDLADGNHGLSSSELAQHVLKKQDL 60
          |||

QUERY: 183 DEDLLGCSPGDLRLRFDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTTVGLSTVLT 242
          |||
20  SBJCT: 61 DEDLLGCSPGDLRLRFDYNSDSSLTLREFYMAFQVVQLSLAPEDRVSVTTTVGLSTVLT 120
          |||

QUERY: 243 CAVHGDRLRPPIIWKRNLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
          |||
25  SBJCT: 121 CAVHGDRLRPPIIWKRNLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 180
          |||

QUERY: 303 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 362
          |||
30  SBJCT: 181 FQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQL 240
          |||

QUERY: 363 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLS 422
          |||
35  SBJCT: 241 SLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTLANILWREEGLS 300
          |||

QUERY: 423 VGNMFYVFSDDGIIIVHPVDCIQRHLKPTKIFMSYEEICPQREKNATQPCQWVSAVNV 482
          |||
40  SBJCT: 301 VGNMFYVFSDDGIIIVHPVDCIQRHLKPTKIFMSYEEICPQREKNATQPCQWVSAVNV 360
          |||

QUERY: 483 RNRYIYVAQPALSRVLVVDIAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 542
          |||
45  SBJCT: 361 RNRYIYVAQPALSRVLVVDIAQKVLQSIGVDPLPAKLSYDKSHDQVWVLSWGDVHKSRP 420
          |||

QUERY: 543 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIFRGFIFNKSDPAVHKVDLETM 602
          |||
50  SBJCT: 421 SLQVITEASTGQSQHLIRTPFAGVDDFFIPPTNLIINHIFRGFIFNKSDPAVHKVDLETM 480
          |||

QUERY: 603 MPLKTIGLHHHGCVQAMAHTHLGGYFFIQCRQDSPASARQLLVDSVTDVLPNGDVT 662
          |||
55  SBJCT: 481 MPLKTIGLHHHGCVQAMAHTHLGGYFFIQCRQDSPASARQLLVDSVTDVLPNGDVT 540
          |||

QUERY: 663 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 722
          |||
60  SBJCT: 541 GTPHTSPDGRFIVSAAADSPWLHVQEITVRGEIQTLYDLQINSGISDLAFQRSFTESNQY 600
          |||

QUERY: 723 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 782
          |||
65  SBJCT: 601 NIYAALHTEPDLLFLELSTGKVGMLKNLKEPPAGPAQPWGGTHRIMRDSGLFGQYLLTPA 660
          |||

QUERY: 783 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 815
          |||
60  SBJCT: 661 RESLFLINGRQNTLRCEVSGIKGGTTVVWVGEV 693
          |||

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      |  |  |  |  |  ++  |  |  |  |  |  +  |  |  |  |  |  +  |  |  |  |  |  |  |  +
SBJCT: 29  CANVFCGAGRECAVTEK-GEPTCLCIEQCKPKRPVCGSNGKTYLNHCELHRDACL TGSK 87

5  QUERY: 98  ITVIHSKDCFLK GDT-----CTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
      |  |  +  |  |  |  |  |  |  |  +  |  +  |  +  +  |  |  |  |  |
SBJCT: 88  IQVDYDGHCKEKK SASPSASPVVCYQANRDELRRRLIQWLEAEIIP----DGWFSKGSNY 143

QUERY: 149  RLLVESLFRDLADGNHGLSSSELAQHVLKK-----QDLDEDLLGCSPGDLLRF 197
      +++  |  +  |  +  |  |  |  |  |  +  |  +  |  |  +  +  |  |  |  +
10  SBJCT: 144  SEILDKYFKSFD-NGDSHLDSEFLKFVEQNETAINITTYADQENNKLLRSLCVDALIEL 202

QUERY: 198  DDYNSDSSLTLREF 211
      |  |  +  |  |  +  |  |
15  SBJCT: 203  SDENADWKLSFQEF 216

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The amino acid sequence of the FCTR2 protein has 63 of 193 amino acid residues (32%) identical to, and 89 of 193 residues (45%) positive with, the 299 amino acid residue protein Follastatin-Related Protein from the African Clawed Frog (GenBank Acc:JG0187) (SEQ ID NO:52) (Table 2I).

Table 2I. BLASTP of FCTR2 against Follastatin-Related Protein from the African Clawed Frog (SEQ ID NO:52)

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>GI|7512162|PIR|JG0187 FOLLISTATIN-RELATED PROTEIN - AFRICAN CLAWED FROG
      LENGTH = 299

25  SCORE = 81.8 BITS (201), EXPECT = 3E-14
      IDENTITIES = 63/193 (32%), POSITIVES = 89/193 (45%), GAPS = 25/193 (12%)

QUERY: 38  CGKKFCRSRGRVLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
      |  |  |  |  |  ++  |  +  |  |  +  |  +  |  |  |  |  +  |  |  |  |  |  +
30  SBJCT: 28  CANVFCGAGRECAVTEK-GDPTCDCEKCKSHKRPVCGSNGKTYLNHCELHRDACL TGSK 86

QUERY: 98  ITVIHSKDCFLK-GDT-----CTMAGYARL-KNVLLALQTRLQPLQEGDSRQDPASQK 148
      |  |  +  |  |  |  |  |  |  |  +  +  +  +  |  |  |  +  |  |  |
35  SBJCT: 87  IQVDYDGHCKEKTSDTPAAVPVACYQSDRDEMRRRVHVLQTEITP----DGWFSKGS DY 142

QUERY: 149  RLLVESLFRDLADGNHGLSSSELAQHVLKKQDL-----DED-----LLGCSPGDLLRFD 198
      +++  |  +  |  |  +  |  |  |  |  +  +  |  |  |  |  |  +  |  |  +
40  SBJCT: 143  SEILDYFKKFD-DGDSHLDSAELQSFLEQSQSTNITTYKDEETNRMLKSLCVEALIELS 201

QUERY: 199  DYNSSDSSLTLREF 211
      |  |  +  |  |  |  |
45  SBJCT: 202  DENADWKLNKNEF 214

```

The amino acid sequence of the FCTR2 protein has 59 of 194 amino acid residues (30%) identical to, and 90 of 194 residues (45%) positive with, the 308 amino acid residue protein Follistatin-Related Protein 1 Precursor from *Homo sapiens* (GenBank Acc:Q12841) (SEQ ID NO:53) (Table 2J).

Table 2J. BLASTP of FCTR2 against Follistatin-Related Protein 1 Precursor from *Homo sapiens* (SEQ ID NO:53)

```

50  >GI|5901956|REF|NP_009016.1| FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
      GI|2498390|SP|Q12841|FRP HUMAN FOLLISTATIN-RELATED PROTEIN 1 PRECURSOR
      GI|1082372|PIR|S51362 FOLLISTATIN-RELATED PROTEIN - HUMAN

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GI|536898|GB|AAA66062.1| (U06863) FOLLISTATIN-RELATED PROTEIN PRECURSOR [HOMO SAPIENS]
GI|3184393|DBJ|BAA28707.1| (D89937) FOLLISTATIN-RELATED PROTEIN (FRP) [HOMO SAPIENS]
5 GI|12652619|GB|AAH00055.1|AAH00055 (BC000055) FOLLISTATIN-LIKE 1 [HOMO SAPIENS]
LENGTH = 308

SCORE = 82.9 BITS (204), EXPECT = 1E-14
10 IDENTITIES = 59/194 (30%), POSITIVES = 90/194 (45%), GAPS = 26/194 (13%)

QUERY: 38 CGKKFCSRGRSRLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
| | | | | ++ | | | | | + | + | | | | | + | | | | | + | | | | | +
SBJCT: 31 CANVFCGAGRECAVTEK-GEPTCLCIEQCKPHKRPVCGSNGKTYLNHCELHRDACLTSK 89

15 QUERY: 98 ITVIHSKDCFLKGD-----TCTMAGYARLKNVLLA-LQTRLQPLQEGDSRQDPASQK 148
| | + | | | | | | | | + + + | + + | | | | |
SBJCT: 90 IQVDYDGHCKEKKSVSPSPVVCYQSNRDELRRRIQWLEAEIIP----DGWFSKGSNY 145

20 QUERY: 149 RLLVESLFRDLADGNHLSSELAQHVLKK-----QDLDEDLLGCSPGDLRLRF 197
+++ |++ | +|+ | | | + | + | + ++ | | | +
SBJCT: 146 SEILDKYFKNFD-NGDSRLDSSEFLKFVEQNETAINITYPDQENKLLRGLCVDALIEL 204

25 QUERY: 198 DDYNSDSSLTLREF 211
| | + | + + |
SBJCT: 205 SDENADWKLSFQEF 218

The amino acid sequence of the FCTR2 protein has 35 of 69 amino acid residues (50%) identical to, and 45 of 69 residues (64%) positive with, the 315 amino acid residue Flik protein [*Gallus gallus*] (EMBL Acc:CAB42968.1) (SEQ ID NO:54) (Table 2K).

30 **Table 2K. BLASTP of FCTR2 against Flik protein [*Gallus gallus*] (SEQ ID NO:54)**

>GI|4837645|EMBL|CAB42968.1| (AJ238977) FLIK PROTEIN [GALLUS GALLUS]
LENGTH = 315

35 SCORE = 79.8 BITS (196), EXPECT = 1E-13
IDENTITIES = 35/69 (50%), POSITIVES = 45/69 (64%), GAPS = 1/69 (1%)

40 QUERY: 38 CGKKFCSRGRSRLSRKTGEPECQCLEACRPSYVPVCGSDGRFYENHCKLHRAACLLGKR 97
| | | | | + | ++ | | | | | + | + | | | | | + | | | | | +
SBJCT: 31 CANVFCGRGAECVTEK-GEPTCLCIEQCKPHGRPVCGSNGKTYLNHCELHRDACLTSK 89

QUERY: 98 ITVIHSKDC 106
| | + |
SBJCT: 90 IQVDYDGHK 98

45 The amino acid sequence of the FCTR2 protein has 49 of 152 amino acid residues (32%) identical to, and 65 of 152 residues (42%) positive with a 272-420 amino acid fragment and, 31 of 83 residues (37%) identical to and 44 of 83 residues (52%) positive with a 248-329 amino acid fragment, both of the 1375 amino acid residue Frazzled gene protein [*Drosophila melanogaster*] (GenBankAcc:T13822) (SEQ ID NO:55) (Table 2L).

50 **Table 2L. BLASTP of FCTR2 against Frazzled gene protein [*Drosophila melanogaster*] (SEQ ID NO:55)**

>GI|7511861|PIR|T13822 FRAZZLED GENE PROTEIN - FRUIT FLY (DROSOPHILA MELANOGASTER)
GI|1621115|GB|AAC47314.1| (U71001) FRAZZLED [DROSOPHILA MELANOGASTER]

LENGTH = 1375

SCORE = 69.4 BITS (169), EXPECT = 2E-10
IDENTITIES = 49/152 (32%), POSITIVES = 65/152 (42%), GAPS = 4/152 (2%)

QUERY: 243 CAVHGDRLRPPIIWKRNGLTINFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
| + | + | | | | + | + | | + | | + | | | | +
SBJCT: 272 CVANGVPKPKQIKWLRNGMDLDFNDLDSRFSIVGTGSLQISSAEDIDSGNYQCRASNTVDS 331

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQ 361
| + | | | | + | + | | | | | | | | ++ |
SBJCT: 332 LDAQATVQVQEPKFIKAPKDDTTAHEKDEPELKCDIWGKPKPVIRWLKNGDLITPNDYMQ 391

QUERY: 362 LSLLANGSELHISSVRYEDTGAYTCIAKNEVG 393
| + | | | + | | + | + | |
SBJCT: 392 ---LVDGHNKILGLLNSDAGMFQCVGTNAAG 420

SCORE = 52.9 BITS (126), EXPECT = 1E-05
IDENTITIES = 31/83 (37%), POSITIVES = 44/83 (52%), GAPS = 2/83 (2%)

QUERY: 311 NVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVS-TQMSKQLSLLANGS 369
+ | | | | + | + | | | + | + | | | + + + ++ | |
SBJCT: 248 SVAPSFVLGSPKTVREGDVTILDCVANGVPKPKQIKWLRNGMDLDFNDLDSRFSIVGTGS 307

QUERY: 370 ELHISSVRYEDTGAYTCIAKNEV 392
| | | | + | | | | |
SBJCT: 308 -LQISSAEDIDSGNYQCRASNTV 329

The amino acid sequence of the FCTR2 protein has 53 of 177 amino acid residues (29%) identical to, and 78 of 177 residues (43%) positive with a 366-539 amino acid fragment, 51 of 170 residues (30%) identical to and 74 of 170 residues (43%) positive with a 276-438 amino acid fragment, 46 of 165 amino acid residues (27%) identical to, and 74 of 165 amino acid residues positive with a 185-341 amino acid fragment, 48 of 167 amino acid residues (28%) identical to and 70 of 167 amino acid residues (41%) positive with a 77-243 amino acid fragment, and 28 of 84 amino acid residues (33%) and 37 of 84 amino acid residues positive with a 56-139 amino acid fragment all of the protein 1395 residue Roundabout 1 protein [*Drosophila melanogaster*] (GenBankAcc:AAC38849.1) (SEQ ID NO:56) (Table 2M).

Table 2M. BLASTP of FCTR2 against Roundabout 1 protein [*Drosophila melanogaster*] (SEQ ID NO:56)

>GI|2804782|GB|AAC38849.1| (AF040989) ROUNDABOUT 1 [DROSOPHILA MELANOGASTER]
LENGTH = 1395

SCORE = 69.8 BITS (170), EXPECT = 1E-10
IDENTITIES = 53/177 (29%), POSITIVES = 78/177 (43%), GAPS = 11/177 (6%)

QUERY: 243 CAVHGDRLRPPIIWKRNGLTINFLDLEDINDF-GEDDSLYITKVTTIHMGNYTCH----- 296
| | + | + | + | + | | + | + | | | | | |
SBJCT: 366 CMASGNPPPSVFWTKEGVSTLMFPNSSHGRQYVAADGTLQITDVRQEDEGYVCSAFSVV 425

QUERY: 297 --SGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDV 354
| | | | + | | | ++ | + | | | | | | | | | + | |
SBJCT: 426 DSSTVRVFLQVSSVDERPPPIIQIGPANQTLPGKSVATLPCRATGNPSPRIKWFDHGHAV 485

QUERY: 355 STQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSARKTL 411
 | + |++ | | + ++ | + | | | | | | ++ | + | + |
 SBJCT: 486 --QAGNRYISII-QGSSLRVDDLQLSDSGTYTCTASGERGETSWAATLTVEKPGSTSL 539

5 SCORE = 56.3 BITS (135), EXPECT = 1E-06
 IDENTITIES = 51/170 (30%), POSITIVES = 74/170 (43%), GAPS = 12/170 (7%)

QUERY: 243 CAVHGDRLPPIIWKRNLTLNFLDLEDINDFGEDDSLYITKVTTIHMGNYTCHASGH-EQ 301
 | + | | | | ++ | | + + ++ | + | | | + + | | | | + |
 10 SBJCT: 276 CSVGGDPPPKVLWKKEEGNIPVSRARILHD---EKSLEISNITPTDEGTIVCEAHNNVGQ 332

QUERY: 302 LFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM--- 358
 + | + | | | | ++ | | | | | + | | | | | | |
 15 SBJCT: 333 ISARASLIVHAPPNFTKRPNSKKVGLNGVVQLPCMASGNPPPSVFWTKEG--VSTLMFPN 390

QUERY: 359 -SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFIEDSA 407
 | + | | | | + | | | | | | + | | + |++ | + |
 SBJCT: 391 SSHGRQYVAADGTLQITDVRQEDGYVCSAFSV--VDSSTVRVFLQVSS 438

20 SCORE = 51.7 BITS (123), EXPECT = 3E-05
 IDENTITIES = 46/165 (27%), POSITIVES = 74/165 (43%), GAPS = 20/165 (12%)

QUERY: 251 PPIIWKRNLTLNFLDLEDINDFG-----EDDSLYITKVTTIHMGNYTCHASG---- 298
 | + | | ++ | + | | + ++ | | + + | | | | | |
 25 SBJCT: 185 PTLIWIKDGVPDL--DLKAMS-FGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGT 241

QUERY: 299 HEQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQM 358
 | + ++ | | | + | | | + | | | | ++ | | ++
 30 SBJCT: 242 RESSYAKLIVQVK--PYFMKEPKDQVMLYGQTATFHCSVGGDPPPKVLWKKEEGNIPVSR 299

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFI 403
 ++ + | + | | ++ | | | | | | | | + | | +
 SBJCT: 300 AR---ILHDEKSLEISNITPTDEGTIVCEAHNNVGQISARASLIV 341

35 SCORE = 44.0 BITS (103), EXPECT = 0.007
 IDENTITIES = 48/167 (28%), POSITIVES = 70/167 (41%), GAPS = 13/167 (7%)

QUERY: 243 CAVHGDRLPPIIWKRNLTLNFLDLEDINDFGEDDSLYITKVTTIHM---GNYTCHASG 298
 | | | | | | ++ | ++ + + + | + | + + | | | |
 40 SBJCT: 77 CKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFFYRTMQGKKEQDGGGEYWCVAKN 136

QUERY: 299 H-EQLFQTHV-LQVNV-PPVIRVYPESQAQEPGVAASLRCH-AEGIPMPRITWLKNGVDV 354
 | | | | | + | | | + | | | | + | | | + | + | + | +
 45 SBJCT: 137 RVQQAQVSRHASLQIAVLRDDFRVEPKDTRVAKGETALLECGPPKGIPEPTLIWIKDGVPL 196

QUERY: 355 STQMSKQLSL-----LANGSELHISSVRYEDTGAYTCIAKNEVGVE 396
 + + + | | | + | | | | | + | | |
 SBJCT: 197 DDLKAMSFAGASSRVRIVDGGNLLISNVEPIDEGNYKCIAQNLVGTRE 243

50 SCORE = 42.9 BITS (100), EXPECT = 0.014
 IDENTITIES = 28/84 (33%), POSITIVES = 37/84 (43%), GAPS = 4/84 (4%)

QUERY: 314 PVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELH- 372
 | | + | + | + | | | | | | + | | | | + | |
 55 SBJCT: 56 PRIIEHPTDLVVKKNEPATLNCKVEGKPEPTIEWFKDGEPVSTNEKKSHRVQFKDGALFF 115

QUERY: 373 ---ISSVRYEDTGAYTCIAKNEVG 393
 + + + | | | + | | | |
 SBJCT: 116 YRTMQGKKEQDGGGEYWCVAKNRVG 139

60

The amino acid sequence of the FCTR2 protein has 55 of 157 amino acid residues (35%) identical to, and 75 of 157 residues (47%) positive with a 620-775 amino acid fragment, 49 of 163 residues (30%) identical to and 71 of 163 residues (43%) positive with a

335-492 amino acid fragment, 32 of 85 amino acid residues (37%) identical to, and 48 of 85 amino acid residues (55%) positive with a 1305-1388 amino acid fragment, 37 of 143 amino acid residues (25%) identical to and 60 of 143 amino acid residues (41%) positive with a 183-319 amino acid fragment, 43 of 174 amino acid residues (24%) and 70 of 174 amino acid residues (39%) positive with a 711-884 amino acid fragment, and 46 of 165 residues (27%) identical to and 69 of 165 residues positive with a 831-884 amino acid fragment all of the protein 1395 residue Down Syndrome Cell Adhesion Molecule Precursor (CHD2) from *Homo Sapiens* (GenBankAcc:O60469) (SEQ ID NO:57) (Table 2N).

Table 2N. BLASTP of FCTR2 against Down Syndrome Cell Adhesion Molecule Precursor (SEQ ID NO:57)

```
>gi|12643619|sp|O60469|DSCA HUMAN DOWN SYNDROME CELL ADHESION MOLECULE PRECURSOR
(CHD2)
GI|6740013|GB|AAF27525.1|AF217525_1 (AF217525) DOWN SYNDROME CELL ADHESION
MOLECULE [HOMO SAPIENS]
      LENGTH = 2012

      SCORE = 70.6 BITS (172), EXPECT = 6E-11
      IDENTITIES = 55/157 (35%), POSITIVES = 75/157 (47%), GAPS = 7/157 (4%)

QUERY: 245 VHGDLRPPIIWKRNGLTNLFLEIDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQ 304
      ||| | |+++| + |++ || |+ ++ +| |||| | +
SBJCT: 620 VSGDLPITITWQKDRPIPGSLGVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAAVE 679

QUERY: 305 THV-LQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-LKNGVDVST---QM 358
      | | ||| | | | | | | | | | | | | | | | | +
SBJCT: 680 HQSQLIVRVPPKPVQPRDQDGIYKGAVILNCSAEGYPVPTIVWKFSGAGVPPQFQPIAL 739

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVD 395
      + ++ +|+||| | | | | | | | | | | | | | |
SBJCT: 740 NGRIQVLSNGS-LLIKHVVEEDSGYYLCKVSNVDGAD 775

      SCORE = 50.6 BITS (120), EXPECT = 7E-05
      IDENTITIES = 49/163 (30%), POSITIVES = 71/163 (43%), GAPS = 16/163 (9%)

QUERY: 243 CAVHGDLRPPIIWKRNGLTNLFLEIDINDFGEDDSLYITKVTTIHMGNYTCHASGHEQL 302
      |+| | | + | ||| || | | | | | | | | | | +
SBJCT: 335 CSVGTGTEDELQELSWYRNGEILNPGKNVRITGINHEN-LIMDHMVKSDGGAYQCFVRKDKLS 393

QUERY: 303 FQTH---VLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITW-----LKNGV 352
      | + ||+ | +| + | + | | | | +| | +| ||| | | |
SBJCT: 394 AQDYVQVLEDGTPKIISAFSE-KVVSAPVSLMCNVKGTPLPTITWTLLDDDPILKGG- 451

QUERY: 353 DVSTQMSKQLSLLAN-GSELHISSVRYEDTGAYTCIAKNEVG 394
      | ++|+ ++ | | | +||| + | | | | | | | |
SBJCT: 452 --SHRISQMITSEGNVVSYLNISSQVRDGGVYRCTANNSAGV 492

      SCORE = 47.9 BITS (113), EXPECT = 5E-04
      IDENTITIES = 32/85 (37%), POSITIVES = 48/85 (55%), GAPS = 6/85 (7%)

QUERY: 333 LRCHAEGIPMPRITWLK--NGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAKN 390
      | | | | | + | +| || | + + | + +||| + | +| + | +| | +||| |
SBJCT: 1305 LPCKAVGDPSPAVKWMKDSNGTSPSLVTIDGRRSIFSNGSFI-IRTVKAEDSGYYSCIANN 1363

QUERY: 391 EVGVDEDISSLFIE---DSARKTLA 412
      | | | | +| ++ | | | ++
SBJCT: 1364 NWGSDEIILNLQVQVPPDQPRLTVS 1388

      SCORE = 42.9 BITS (100), EXPECT = 0.015
```

IDENTITIES = 37/143 (25%), POSITIVES = 60/143 (41%), GAPS = 6/143 (4%)

QUERY: 270 INDFGEDDSLYITKVTTIHMGNYTCHASGHEQLFQTHVLQVNVPPVIRVYPESQAQEPGV 329
 SBJCT: 183 IKDVQNEEDGLYNYRCITRHRYTGETRQSN SARLFVSD--PANSAPSILDGFDHRKAMAGQ 240

QUERY: 330 AASLRCHAEGIPMPRITWLKNGVDVSTQMSKQLSLLANGSELHISSVRYEDTGAYTCIAK 389
 SBJCT: 241 RVELPCKALGHPEPDYRWLKD--NMPELSGRFQKTVTG--LLIENIRPSDSGSYVCEVS 296

QUERY: 390 NEVGVEDISSLFIEDSARKTLA 412
 SBJCT: 297 NRYGTAKVIGRLYVKQPLKATIS 319

SCORE = 41.3 BITS (96), EXPECT = 0.047
 IDENTITIES = 43/174 (24%), POSITIVES = 70/174 (39%), GAPS = 11/174 (6%)

QUERY: 243 CAVHGDLRPPPIIWK--RNLGLTLNF--LDLEDINDFGEDDSLYITKVTTIHMGNYTCHASG 298
 SBJCT: 711 CSAEGYPVPTIVWKFSGAGVPPQFQPIALNGRIQVLSNGSLLIKHVVEEDSGYYLCKVSN 770

QUERY: 299 H--EQLFQTHVLQVNVPPVIRVYPESQAQEPGVAASLRCHAEGIPMPRITWLKNGVDVST 356
 SBJCT: 771 DVGADVSKSMYLTVKIPAMITSYPNTTLATQGGKEMSCCTAHGEKPIIVRWEKEDRIINP 830

QUERY: 357 QMSKQLSLLANGSELHISSVRY-----EDTGAYTCIAKNEVGVEDISSLFIED 405
 SBJCT: 831 EMARYLVSTKEVGEEVISTLQILPTVREDSGFFSCHAINS YGEDRGIIQLTVQE 884

SCORE = 40.6 BITS (94), EXPECT = 0.074
 IDENTITIES = 46/165 (27%), POSITIVES = 69/165 (40%), GAPS = 7/165 (4%)

QUERY: 243 CAVHGDLRPPPIIWKRNLGLTLNFDLEDINDFGEDDSLYITKVTT-IHMGNYTCHASGHEQ 301
 SBJCT: 525 CRVIGYPYYSIKWYKNSNLLPFNHRQVA--FENNGTLKLSDVQKEVDEGEYTCNVLVQPQ 582

QUERY: 302 LFQTHVLQVN--VPPVIRVYPESQAQEPGVAASLRCHAEGIPMP-RITWLKNGVDVSTQM 358
 SBJCT: 583 LSTSQSQSVHVTVKVPPFIQPF-EFPRFSIGQRFVPCVVVSGDLPITITWQKDRPIPGSL 641

QUERY: 359 SKQLSLLANGSELHISSVRYEDTGAYTCIAKNEVGVEDISSLFI 403
 SBJCT: 642 GVTIDNIDFTSSLRISNLSLMHNGNYTCIARNEAAVEHQSQLIV 686

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Homo sapiens* (SWISSPROT Acc:Q13449) (SEQ ID NO:58) (Table 20).

Table 20. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (SEQ ID NO:58)

PTNR:SWISSPROT-ACC:Q13449 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR (LSAMP) - HOMO SAPIENS (HUMAN), 338 AA.

LENGTH = 338

SCORE = 191 (67.2 BITS), EXPECT = 6.7E-12, P = 6.7E-12
 IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

The amino acid sequence of the FCTR2 protein has 68 of 190 amino acid residues (35%) identical to, and 92 of 190 residues (48%) positive with Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SPTREMBL Acc:O70246) (SEQ ID NO:59) (Table 2P).

Table 2P. BLASTP of FCTR2 against Putative Neuronal Cell Adhesion Molecule, Short Form from *Mus musculus* (SEQ ID NO:59)

PTNR:SPTREMBL-ACC:O70246 PUTATIVE NEURONAL CELL ADHESION MOLECULE (PUNC) (PUTATIVE NEURONAL CELL ADHESION MOLECULE, SHORT FORM) - MUS MUSCULUS (MOUSE), 793 AA

LENGTH = 793

SCORE = 203 (71.5 BITS), EXPECT = 7.0E-12, SUM P(2) = 7.0E-12
IDENTITIES = 68/190 (35%), POSITIVES = 92/190 (48%)

The amino acid sequence of the FCTR2 protein has 58 of 199 amino acid residues (29%) identical to, and 91 of 199 residues (45%) positive with CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SPTREMBL Acc: O02869) (SEQ ID NO:60) (Table 2Q).

Table 2Q. BLASTP of FCTR2 against CHLAMP, G11-Isoform Precursor from *Gallus gallus* (SEQ ID NO:60)

PTNR:SPTREMBL-ACC:O02869 CHLAMP, G11-ISOFORM PRECURSOR - GALLUS GALLUS (CHICKEN), 350 AA.

LENGTH = 350

SCORE = 191 (67.2 BITS), EXPECT = 7.7E-12, P = 7.7E-12
IDENTITIES = 58/199 (29%), POSITIVES = 91/199 (45%)

The amino acid sequence of the FCTR2 protein has 55 of 194 amino acid residues (28%) identical to, and 86 of 194 residues (44%) positive with Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SWISSPROT Acc:Q62813) (SEQ ID NO:61) (Table 2R).

Table 2R. BLASTP of FCTR2 against Limbic System-Associated Membrane Protein Precursor (LSAMP) from *Rattus norvegicus* (SEQ ID NO:61)

PTNR:SWISSPROT-ACC:Q62813 LIMBIC SYSTEM-ASSOCIATED MEMBRANE PROTEIN PRECURSOR (LSAMP) - RATTUS NORVEGICUS (RAT), 338 AA.

LENGTH = 338

SCORE = 188 (66.2 BITS), EXPECT = 1.5E-11, P = 1.5E-11
IDENTITIES = 55/194 (28%), POSITIVES = 86/194 (44%)

FCTR2 protein has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Frazzled encodes a *Drosophila* member of the DCC

immunoglobulin subfamily and is required for CNS and motor axon guidance (Cell 87:197-204(1996)). Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP) and cloning and sequence of the human homologue is described in Eur. J. Biochem. 225:937-946(1994). This protein may modulate the action of some growth factors on cell proliferation and differentiation. FRP binds heparin. The follistatin-related protein is a secreted protein and has one follistatin-like domain. The cloning and early dorsal axial expression of Flik, a chick follistatin-related gene and evidence for involvement in dorsalization/neural induction is presented in Dev. Biol. 178:327-342(1996). Roundabout controls axon crossing of the CNS midline and defines a novel subfamily of evolutionarily conserved guidance receptors, as shown in Cell 92:205-215(1998). cDNA cloning and structural analysis of the human limbic-system-associated membrane protein (LAMP) is described in Gene 170:189-195(1996). LAMP, a protein of the OBCAM family that contains three immunoglobulin-like C2-type domains, mediates selective neuronal growth and axon targeting. LAMP contributes to the guidance of developing axons and remodeling of mature circuits in the limbic system. This protein is essential for normal growth of the hippocampal mossy fiber projection. LAMP is attached to the membrane by a GPI-Anchor. It is expressed on limbic neurons and fiber tracts as well as in single layers of the superior colliculus, spinal chord and cerebellum. Characterization of the human full-length PTK7 cDNA encoding a receptor protein tyrosine kinase-like molecule closely related to chick KLG is disclosed in J. Biochem. 119:235-239(1996). Based upon homology, FCTR2 proteins and each homologous protein or peptide may share at least some activity.

Functions and therapeutic uses:

The OMIM gene map has identified this region which the invention maps to (5q21-5q31) as associated with susceptibility to the following diseases (OMIM Ids are underlined):

- Allergy and asthma
- Hemangioma,
- capillary infantile Schistosoma mansoni infection, susceptibility/resistance to Spinocerebellar ataxia
- Bronchial asthma
- Plasmodium falciparum parasitemia,
- intensity of Corneal dystrophy, Groenouw type I, 121900; Corneal dystrophy, lattice type I, 122200;

T00001" 86T00860

- Reis-Bucklers corneal dystrophy;Corneal dystrophy, Avellino type Eosinophilia, familial Myelodysplastic syndrome;
- Myelogenous leukemia, Acute Cutis laxa, recessive, type I, Deafness, autosomal dominant nonsyndromic sensorineural, 1 Contractural arachnodactyly, Congenital Neonatal alloimmune thrombocytopenia;
- Glycoprotein Ia deficiency Male infertility;
- Charcot-Marie-Tooth neuropathy, Demyelinating Gardner syndrome ;
- Adenomatous polyposis coli;
- Colorectal cancer;
- Desmoid disease, hereditary, 135290;
- Turcot syndrome,276300;
- Adenomatous polyposis coli, attenuated
- Colorectal cancer

Therefore the invention is implicated in at least all of the above mentioned diseases and may have therapeutic uses for these diseases.

This sequence has similarity to cell adhesion molecules, follistatin, roundabout and frazzled (see BlastP results). These genes are involved in neuronal development and reproductive physiology. Therefore the invention is also implicated in disorders such as therapeutic uses for:

- Neurodegenerative disorders, nerve trauma, epilepsy, mental health conditions
- Tissue regeneration in vivo and in vitro

Female reproductive system disorders and pregnancy

FCTR3

FCTR3, is an amino acid type II membrane, neurestin-like protein. The FCTR3a nucleic acid of 1430 nucleotides (also designated 10129612.0.118) is shown in Table 3A. An ORF was identified beginning with an ATG initiation codon at nucleotides 69-71 and ending with a TAG codon at nucleotides 1212-1214. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3A, and the start and stop codons are in bold letters.

Table 3A. FCTR3a Nucleotide Sequence (SEQ ID NO:5)

5 AAAAAAGGCGGGGGTGGACTTAGCAGTGAATTTGAGACCGGTGGTAAGGATTGGAGCGAGCTAGAGATGCTGCACGCTGCTA
 ACAAGGGAAGGAAGCCTTCAGCTGAGGCAGGTCGTCCCATTCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGC
 CTAGCTCCCATATCCTCCACCACTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACC
 CTGATGAGGAATTCCTCCCAATTCATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACC
 ACCACAGCCAGTCCGACTCTGAGGCCCTCTCCACCCCTCACAACCACACGCTGTCCCATCACCCTCGTCCGCCAATCCC
 TCAACAGGAACCTCACTGACCAATCGGCGGAGTCAGATCCACGCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACAGAGT
 CCGTTCAGCTTCAGGACAGCTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCCTCTCAAGACCTCCTCGGGGA
 GCACACCTTTGTTAGCAGCTCTCCCCGGGATACCTTTGACCTCAGGAACGGTTTACACGCCCGCCCGCCCTGCTGCCCA
 10 GGAATACTTTCTCAGGAAGGCTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAATGTGCTGCCCTCTCCGCCATTG
 CCGCGGCCCTCCTCTTGCTATTTTGCTGGCGTATTTATAGTGGCCCTGGTTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAG
 CAGAAGTTGGTGGCGGGTAACACAAGAAGTCCACCAGGGGTGTTTGGAGGTCAAAATTCACATCAGTCAGCCCCAGTTCT
 TAAAGTTCAACATCTCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCATGCCAGTATG
 ACTTCATGGAACGCTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATACAGACCTTGGTTC
 15 AGAATGAAGCCGTGTTTGTGTCAGTACCTGGATGTGGCCCTGTGGCATCTGGCCTTCTACAATGATGGAAGCAAGAGATGG
 TTTCTTCAATACTGTTGTCTAGATGGGACCATCTAGTTGCAGAAAAACAAGCTCAGGGCGCCCACTGATTGACATTATGAT
 TCAGTGCAGGACTGTCCACGTAACGCCATGGGAATGGTGAATGTGTGTCCGGGTGTGTCAGTGTTCACAGATTTCTAGGA
 GCAGACTGTGCTAAAGACCTTCCTGCCTTGACTTTCTGCAAGACAATCATTAATAAAGCTGCTCTGTAAATACTAAAAA
 CA

The FCTR3 polypeptide (SEQ ID NO:5) encoded by SEQ ID NO:5 is 381 amino acid residues and is presented using the one-letter code in Table 3B.

Table 3B. Encoded FCTR3a protein sequence (SEQ ID NO:6).

25 MLHAANKGRKPSAEAGRPIPTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSNPSYLLRACSGPQQASS
 SGPPNHHSQSTLRPPLPPPHNHTLSHHSSANSNLNRSLTNRRSQIHAPAPAPNDLATTPEVQLQDSWVLNSNVPLETRHFLF
 KTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLPRNTFSRKAFKLKPKSKYCSWKCAALSAIAAALLLAILLAYFIVPWSLKNSS
 IDSGEAEVGRVRVTQEVPPGVFWRQIHSQPQFLKFNISLGKDALFGVYIRGLPPSHAQYDFMERLDGKEKWSVVESEPRERS
 IQTLVQNEAVFVQYLDVGLWHLAFYNDGDKDEMVSFNTVVLDTGT

30 In an alternative embodiment, the 5' end of the FCTR3a nucleic acid could be extended as it is in the 9826bp FCTR3b (also referred to herein as 10129612.0.405) shown in Table 3C. An ORF was identified beginning with an ATG initiation codon at nucleotides 280-282 and ending with a TAA codon at nucleotides 8479-8481. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3C, and the start and stop codons are in bold letters. Italicized bases 1-201 refer to a variable 5' region that will be further discussed below.

Table 3C. FCTR3b Nucleotide Sequence (SEQ ID NO:7)

40 TTTAAATCCTCATACCTTAAAGGAGATGTGTATATAAGGGAGTTGGAAACGACATTAGATGAGTTGACAAAAATGCAGTT
TCAGTTCTAGAGGTCTGGGAAGTCCAAGAAACAAGGTGCTGGCAGATTGGATTCCCCGTGAGGGCTTTCTCTCGGCTTGA
AGTTGGCTGCTTTCTGCTGAGACTTCTCATGGCAGAGACTGAGGGTGGCAAAGTGACAAGTGCCAAACTCAGGCCTGA
CTTTTCTGAAAACATCAGCATCTCTGCCATATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGG
 ACCTGTGGCAAAGAGTGTCTGTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACAGAAATCCTACA
 GCTCCAGTGAGACTCTGAAGGCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACCGG
 GAGTCAGATGAGTTTCTAGACAAGGAACCAACTTACCCCTTGGCGAAGTGGGCATCTGTGAGCCCTCCCCACACCGAAG
 45 CGGCTACTGCTCCGACATGGGGATCCTTACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGG
 GAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTCGT
 GAAAACTCGGCCCTTACCCTGACTGACTCTGACAACGAAACAAATCAGATGATGAGAACGGTCGTCCCATTCACCTAC
 ATCCTCGCCTAGTCTCCTCCATCTGCTCAGCTGCCTAGTCCCATTAATCCTCCACCAAGTGTGCTGCCAGATGCCATTGC
 TAGACAGCAACACCTCCCATCAAATCATGGACACCAACCTGATGAGGAATTTCTCCCAATTATACCTGCTCAGAGCA
 50 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACACAGCCAGTCTGAGTCTGAGGCCCTCTCCACCC
 CCCTCACAACACACGCTGTCCCATCACCCTCGTCCGCCAATCCCTCAACAGGAATCACTGACCAATCGGCGGAGTC
 AGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACAGAGTCCGTTTACGCTTCAGGACAGCTGGGTGCTA

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15966-697

[illegible]

The FCTR3b polypeptide (SEQ ID NO:8) encoded by SEQ ID NO:7 is 2733 amino acid residues and is presented using the one-letter code in Table 3D. The protein has a predicted molecular weight of 303424.3 daltons.

MDVKKDRHRSLSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAE
LGICEPSPHRSGYCSDMGILHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTDSNENKSDDE
NGRPIPTTSSPSLLPSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFPSPNSYLLRACSGPQOASSSGPPNHHSQSTLR
PPLPPPNNHTLSHHSSANSLSLRNSTLTNRSSQIHAPAPAPNDLATTPESVQLQDSWVLNNVPLETRHFLFKTTSSSGSTPLFSS
SSPGYELTSGVTYTPPRLHPPLNTFSRKAFKLKPKSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRR
VTOEVPVPGVFWRSQTHISLQPOFLKFNISLKGDAALFGVYIRRGLEPPSHAQYDFMERLGDKEKWSVSPERRRSTQTLVQNEAV
FVQYLDVGLWHLAFYNDGDKDEMVSFNTVVLDSVQDCPRNCHNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTC
QCYSGWKGAECVPMNQCIDPSCGGHGSCIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQ
CPDQCSGHGTYLPTDGLCSDPNWMPGDCSVEVCSVDGCTHGVICIGACRCEEWGTAACDQRVCHPRCIEHGTCKDGKCECR
EGWNGEHCTIGRQTAGTETDGCPLDCNGNCRCTLQNSQVCQVCTGWRGPGCNVAMETSCADNKNEDGDLVCLDPCCLQS
ACQNSLLCRGSRPLDIIQQGQTDWPAVKSFYDRIKLLAGKSDTHIIPGENPFNSLSVLIRGQVTTDGTPLVGNVSVFVKY
PKYGYTTITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLMKTEENSIPSCDLSGFFVRPDPPIISSPLS
TFFSAAPGQNPPIVPETQVLHEEIELPGSNVKLRYLSSRTAGYKSLKTI MTQSTVPLNLRVHLMVAVEGHLFQKSFQASP NL
ASTFIWDKTDAYGQRVYGLSDAVVSGFYEYTCPSSLILWEKRTALLQGFE LDP SNLGGWSLDKHHILNVKSGILHKGKGTENQF
LTQQPAIITSIMGNRRRSISPCSCNGLAEAGNKLALVALAVAGIDGSLYVGDFNYIRRIFFSRNNVSI LELNRKEFKHNSNP
HKYYLAVDPVSGSLYVSDTNSRRIYRVKLSGTDKLAGNSEVAGTGEQCLPFEARCGDGKKAIDATLMSPRGIAVDKXNGLM
YFV DATMTIRKVDQNGIISTLLGNSDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGR

PMHCQVPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINRLRQVTTNGEICLLAGAASDCDCCKNDVNCNCYSGDD
 AYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPEQEQLYVFNADGIHQYTVSLVTGEYLYNFT
 YSTDNDVTELIDNNGNSLKIRDDSSGMPRHLLMPDNQIITLTVTGNGGLKVVSTQNLGLMTYDGNTGLLATKSDGTGWTTF
 YDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGM
 5 GISFHESEPHVLAGTITPTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKF
 TLRIIYDQVGRPFLLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLQSQRO
 YIFEDSSDRLLAVTMPSPVARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRILKTSFLGTGRQVFKYKGLSKLSEIVY
 DSTAVTFGYDETTGVLKMNVLQSGGFSCITRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDL
 10 YRYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPYANTT
 KYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHLLNPGNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQGRGSDIFEYNS
 KGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHNSNBITSLSYYDLQGHLFAMESSSGEEY
 YVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNV
 GKEPAPFNLYMFKSNPLSSELDLKNYVTDVKSWMVFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTE
 15 RHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIE
 GKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFYSTLLLSIRYGLTPDLDDEEKARVLD
 QARQALGTAWAKEQQKARDGREGRSLWTEGEKQQLLSTGRVQGYEGYVLPVEQYPELADSSSNIQFLRQNMGRK

In further alternative embodiments the italicized bases in the 5' end of the FCTR3b
 sequence in table 3C is a variable region. This region can be substituted for in other
 20 embodiments of FCTR3. The nucleotide sequence for 9823bp FCTR3c (also referred to
 herein as 10129612.0.154) has the same nucleotide sequence as FCTR3b except that the
 italicized region is replaced with the 201 base sequence shown in Table 3E. An ORF for the
 total FCTR3c nucleotide sequence was identified beginning with an ATG initiation codon at
 nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-8475. This is the
 25 same open reading frame that is shown in Table 3C, with the corresponding base numbers for
 FCTR3c. This open reading frame will translate the same amino acid sequence as shown in
 Table 3C for FCTR3b.

Table 3E. Encoded FCTR3c 5'end nucleotide sequence (SEQ ID NO:9).

30 GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTGAGGAGCGAAGCTACTGACCGA
 GCTGCTGTACATCCAGCTTTTAAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
 TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence
 35 in Table 3C can be replaced with the sequence shown in Table 3F to form 9823bp FCTR3d
 (also referred to herein as 10129612.0.67). An ORF was identified beginning with an ATG
 initiation codon at nucleotides 277-280 and ending with a TAG codon at nucleotides 8473-
 8475. This is the same open reading frame that is shown in Table 3C, with the corresponding
 base numbers for FCTR3d. This open reading frame will translate the same amino acid
 40 sequence as shown in Table 3D for FCTR3b.

Table 3F. Encoded FCTR3d 5'end nucleotide sequence (SEQ ID NO:10).

45 GCTCCAAAGCGAGCTGGGACCGAAGACTCTAGGCTAAGTTATCTATGTAGATGGTGTGAGGAGCGAAGCTACTGACCGA
 GCTGCTGTACATCCAGCTTTTAAATTGCCTAAGCGGTCTGGGGCTTGCTTCGTCATTTGGCTTTGCTGTGGAGCACTCC
 TGTAAGCCAGCTGAATTGTACATCGAAGATCCACCCCTTTT

In yet another embodiment, the italicized region shown in the 5' end of the sequence in Table 3C can be replaced with the sequence shown in Table 3G to form 9765 bp FCTR3e (also referred to as 10129612.0.258). An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8408-8410. This is the same open reading frame that is shown in Table 3C, with the corresponding base numbers for FCTR3e. This open reading frame will translate the same amino acid sequence as shown in Table 3D for FCTR3b.

Table 3G. Encoded FCTR3e 5'end nucleotide sequence (SEQ ID NO:11).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA
TTCTGCTACAACATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAA

In yet another embodiment another FCTR3a homolog, FCTR3f (also referred to as 10129612.0.352) was found having the 9729bp sequence shown in Table 3H. An ORF was identified beginning with an ATG initiation codon at nucleotides 210-212 and ending with a TAG codon at nucleotides 8382-8384. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 3G, and the start and stop codons are in bold letters.

Table 3H. Encoded FCTR3f nucleotide sequence (SEQ ID NO:12).

CCAGCATTAGATGAGTTGACAAAAATGCAGTTTCAGCTCTGAAGGTCTGAAAGATTCTGCTGCAACTAAAGCTCTGAAGA
TTCTGCTACAACATGACATCCATTTTCTCCCACTTCAGACAGGATGAATACAAAGTGGCAAAGTGACAAGTGCCAAAAC
TCAGGCTGACTTTCCTGAAAACATCAGCATCTGCGCATATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTT
TGACCAAGGACGCTGTGGCAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACAG
AAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTATGAAACCGAGTCACAGACCT
CATCCACCGGGAGTCAGATGAGTTTCTAGACAAGGAACCAACTTCACCTTGCCGAAGTGGGCATCTGTGAGCCCTCCC
CACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTCC
GACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCT
GTCCAGTCGTGAAAACCTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGATGAGAACGGTCTGCCA
TTCCACCTACATCCTCGCCTAGTCTCCTCCCCTCTGCTCAGCTGCCTAGCTCCCATATCCTCCACAGTTAGCTGCCAG
ATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCTGATGAGGAATCTCCCCCAATTATACCT
GCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCTCCGAACACCACAGCCAGTCGACTCTGAGGCCCC
CTCTCCACACCCCTCACAACACACGCTGTCCCATCAGACTCGTCCGCCAACTCCCTCAACAGGAACCTCAGCCCAAT
CGGCGGAGTCAGATCCACGCCCCCGGCCAGCGCCCAATGACCTGGCCACCACACAGAGTCCGTTACAGTTTCAGGACAG
CTGGGTGCTAAACAGCAACGTGCCACTGGAGACCCGGCACTTCTCTTCAAGACCTCCTCGGGAGCACACCTTGTTC
GCAGCTCTTCCCCGGGATACCTTTGACCTCAGGAACCGTTTACACGCCCCCGCCCCGCTGCTGCCAGGAATACTTTT
TCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAATGTGCTGCCCTCTCCGCCATTGCCCGGG
CCTCCTCTTGGCTATTTTGTGGCGTATTTTCAATAGTGCCCTGGTCTGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAG
AAGTTGGTTCGGCGGGTAACACAAGAAGTCCACACAGGGGTGTTTGGAGGTCAAAATTCACATCAGTCAGCCCCAGTTC
TTAAAGTTCAACATCTCCCTCGGAAGGACGCTCTCTTTGGTGTTCATATAAGAAGAGGACTTCCACCATCTCATGCCCA
GTATGACTTCATGGAACGCTCGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGGAGCATACAGA
CCTTGGTTTCAAGTGAAGCCGTGTTTGTGCACTACCTGGATGTGGCCCTGTGGCATCTGGCCTTCTACAATGATGAAAA
GTGGAATGGACAATATTCTAAAGGACGTGCCAGTGCTACAGCGGCTGGAAGGTGCAGAGTGGCAGCTGCCATGGGAATGGTGA
ATGTGTGTCCGGGTGTGTCACTGTTTCCAGGATTTCTAGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCA
GTGGGAATGGACAATATTCTAAAGGACGTGCCAGTGCTACAGCGGCTGGAAGGTGCAGAGTGGCAGCTGCCATGGGAATGGTGA
CAGTGATCGATCCTTCTCGGGGGCCACGGCTCCTGCATTGATGGGAACGTGTGTCTGCTCTGCTGGCTACAAAGGCGA
GCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCC
CTGGCTGGGTGGTCTGAACGTGTGAGCTGGCGAGGGTCCAGTGGCCAGACAGTGCAGTGGGCATGGCAGCTACCTGCCCT
GACACGGGCTCTGCAGCTGCGATCCCACTGGATGGGTCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGTGGCAC
TCACGGCTGTGCATCGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGGTGTGCCACC
CCCGCTGCATTGAGCATGGGACCTGTAAAGATGGCAAATGTGAATGCCAGAGGGGTGGAATGGTGAACACTGCACCATT
GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGGCAGTGTGTCTGCCAGACCGG

CTGGAGAGGGCCCGGATGCAACGTTGCCATGGAACCTTCTGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGG
ATTGTTTGGACCTGACTGCTGCTGCAGTCAGCCTGTGAGAACAGCCTGCTGCGGGGGTCCCGGACCCACTGGAC
ATCATTAGCAGAGGGCCAGACGGATTGGCCCGCAGTGAAGTCTTCTATGACCGTATCAAGCTCTTGGCAGGCAAGGATAG
5 CACCACATCATCTCTGGAGAGAACCTTTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCAAGTAGTAACACAGATG
GAATCCCCCTGGTGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCAGC
TTCGACCTGATCGAAATGGAGGTGCTTCTTGACTCTACACTTTGAGCGAGCCCGTTTATGAGCCAGGAGCGCACTGT
GTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCCCTGGTGTATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACC
10 TCAGTGGCTTTGTCCGGCTGATCCAATCATCATCTCTCCCACTGTCCACCTTCTTTAGTGTGCCCCCTGGGCAGAAT
CCCATCGTGCCTGAGACCCAGGTTCTTATGAAGAAATCGAGCTCCCTGGTTCCAATGTGAAACTTCGCTATCTGAGCTC
TAGAACTGCAGGGTACAAGTCACTGCTGAAGATCACCATGACCCAGTCCACAGTGCCCCCTGAACCTCATTAGGGTTTACC
TGATGGTGGCTGTCGAGGGGCATCTCTTCCAGAAGTCACTCCAGGCTTCTCCCACTGGCTCCACCTTCACTTGGGAC
AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTGCGGTTTGAATATGAGACCTGTCC
CAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCTTTCAGGGATTGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCC
15 TAGACAAAACACCATCTCAATGTAAAAGTGAATCCTACACAAAGGCACTGGGGAAAACAGTTCTGACCCAGCAG
CCTGCCATCATCACCAGCATCATGGGCAATGGTCCGCCCGGAGCATTTCTGTCCCAGCTGCAACGGCCTTGTGAAGG
CAACAAGCTCTGGCCCCAGTGGCTCTGGCTGTTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGAC
GCATCTTTCCCTCTCGAAATGTGACACGATCTTGGAGTTACGAAATAAGAGTTTAAACATAGCAACAACCCAGCACAC
AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCTCAA
20 GTCTCTGAGTGAACCAAGACCTGGCTGGGAATTCCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCTTTGATG
AAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG
CTCATGTACTTTGTGATGCCACCATGATCCGGAAGTTGACCAAGATGGAATCATCTCCACCTGTGGGCTCCAATGA
CCTCACTGCGCTCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGTGAGTGGCCAACAGACCTTG
CTGTCAATCCCATGGATAACTCCTTGTATGTTCTAGAGAACAATGTCTCTTCAATCACCGAGAACCCAAAGTCAGC
25 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCTTGGCATTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCT
GGAGTCAGCCAGTGCCATTGCCATTCTCACACTGGGGTCTCTACATCACTGAGACAGATGAGAAGAAGATTAAACGCTC
TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGATGCAAAAACGATGTCAAT
TGCAACTGCTATTTCAGGAGATGATGCCATACGCACTGATGCCATCTTGAATTCCCCATCATCTTAGCTGTAGCTCCAGA
TGGTACCATTTCATTGACAGCCTTGGAAATATTCCGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCTTAATGCCTTCA
30 ACCAGTATGAGGTGTCATCCCCCGGAGAGCAGGAGTTATATGTTTCAACGCTGATGGCATCCACCAATACATGTGAGC
CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAA
TTCCTGAAGATCCGTGCGGACAGCAGTGCCTGCCCCGTGCTGCTCATGCTGACACACAGATCATCAACCTCACCG
TGGGCACCAATGGAGGCCCTCAAAGTCGTGTCCACACAGAACCCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG
CTCCTGGCCACCAAGAGCGATGAACAGGATGGACGACTTTCTATGACTATGACCAGAAAGCCGCTGACCAACGTCAG
35 GCGCCCCACGGGGGTGGTAACAGTCTGCACCGGGAATGGAGAAATCTATTACCATTTGACATTGAGAACTCCAACCGTG
ATGATGACGTCACTGTATCAACACCTCTCTTCACTAGAGGCTCTTACACAGTGGTACAAGATCAAGTTCCGGAACAGC
TACAGCTCTGTAATAATGTTACCCCTGAGGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCATGT
CCTAGCGGGACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGT
GGCGCCTAAGAAAGGAACAGATTAAAGGCAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG
40 TCCATTGACTATGATCGAAATATTCCGACTGAAAAGATCTATGATGACCACCGGAAGTTACCCCTGAGGATCATTATGA
CCAGGTGGGCGCCCCCTCTCTGGCTGCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTTCAATGGGCGCC
TGGCTGGGCTTACGCGTGGGGCCATGACGAGAGGACAGACATCGACAAGCAAGGCGCATCGTGTCCGCTGCTCGCT
GACGGGAAAGTGTGGAGCTACTCTTACCTTGACAAGTCCATGGTCTCTGCTTTCAGAGCCAACGTGAGTATATATTGA
GTATGACTCTCTGACCGCCTCTTGGCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCG
45 GCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCCGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG
AAGACCTCTTTTGGGACCCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAGTTATCAGAGATTGTCTACGA
CAGTACCGCGCTGACCTTCCGGTATGACGAGAGCCACTGTGCTTGAAGATGGTCAACCTCCAAGTGGGGGCTCTCTCT
GCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC
AGGTTTGTACTACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATAAGTGAGACTCCCCTCCCCGT
50 TGACCTCTACCGCTATGATGAGATTCTTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACC
AGATATCACCACTGCCGTGATGACCTCAGCAAACTCTGACACCCATGGGCGGATCAAGGAGTCCAGTATGAGATG
TTCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGTATCAAGAGGAGCTAAAACCTGGGGCC
CTATGCCAATACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCGCTCAATGACCGCCCGA
CCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC
55 TATGACCTCCGGGATCGGATAACAGACTCGGGGATGTGCGAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGG
GTCTGACATCTTCAATAACAATTCAAAGGGCTCTTACAAGAGCCTACAACAAGGCCAGGGGTGGAGTGTCCAGTACC
GCTATGATGGCGTAGGACGGCGGGCTTCTTACAAGAACCTGGGCCACCACTGCAGTACTTCACTCTGACCTGCCAC
AACCCGACGCGCATCACCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCT
CTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTGAGCA
60 TCAACGGCCTCATGATCAAAACAGCTGCAGTACACGGCCTATGGGGAGATTATATGACTCCAACCCGACTTCCAGATG
GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGC
AGGACGATGGACCTCCCGAGACTATACCATGTGGGAAAACAGCTGGGCAAGGAGCCGGCCCCCTTAAACCTGTATATGTTCA
AGAGCAACAATCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGA
TTTCAGCTTAGCAACATCATTCTGGCTTCCCGAGAGCCAAAATGTATTTCTGTCCTCTCCCTATGAATTTGTGAGAGAG
65 TCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACAGGCCCTTCATGGCTCTGG
AAGGACAGGTCACTACTAAAAGCTCCAGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGGCAACCAACGCCCCATC
ATTGGCAAAAGGCATCATGTTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCG
CAAGGTGGCATCTGTGCTGAACAACGCCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACT
TTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACTAGGCACCAACATCGGCCGAAGGTGCTAGAGAGCGGGGTG

AACGTGACCGTGTCCCAGCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCAGTACTCCAC
GCTGCTGCTCAGCATCCGCTATGGCCTCACCCCGACACCTGGACGAAGAGAAGGCCCGCTCTGGACCAGGCGAGAC
AGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGACGGGAGAGAGGGGAGCCGCTGTGGACTGAG
GGCGAGAAGCAGCAGCTTCTGAGCACGGGCGCGTGAAGGGTACGAGGGATATTACGTGCTTCCCGTGGAGCAATACCC
5 AGAGCTTGCAGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGC
CATTCCTTGTCTGAATGGCTCAGCAGGAGTAACCTGTTATCTCTCTCTAAGGAGATGAAGACCTAACAGGGCCTGGC
GCTGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGTAGTTCAAATGCTACTGTCCAAGCAGAGAAGTCC
CTCATCTGAAGTAGACTAAAGCCCGGCTGAAAATTCGAGGAAAACAAAACAAACGAATGAATGAACAGACACACACAA
10 TGTTCGAAGTTCCTTAAATATGACCCACTTGTCTGGGTCTACGCAGAAAAGAGACGCAAAGTGTCCAAAGGAACAA
AAGAACAAAACGAATAAGCAAGAAGAAAACAAAACAAAACAAAACACACGGACCGATAAACAAAGAAGC
GAAGATAAGAAAGAAGGCTCATATCCAATTACCTCACTCATTCACATGTGAGCGACACGACAGACATCCGCCAGGGCCAG
CGTCACCAGACCAGCTGCGGGACAAACCACTCAGACTGCTTGTAGGACAAATACTTCTGACATTTTCGTTTAAACAAATA
CAGGTGCATTTAAACACGACTTTGGGGGTGATTTGTGTGTAGCGCTGGGGAGGGGGGATAAAAGAGGAGGAGTGTAGCA
CTGGAAATACTTTTTAAAGAAAAAAAACATGAGGGAATAAAAGAAATTCCTATCAAAATCAAAAGTGAAATAATACCAT
15 CCAGCACTTAATCTCAGGTCCCACTAAGTCTGGCCTGAGCTAATTTATTTGAGCGCAGAGTGTAAAATTTAATTCAAA
ATGGTGGCTATAACTACTACAGATAAATTCATACACTCTTTTGTCTTTGGAGATTCCATTGTGGACAGTAATACGCAAGTTA
CAGGGTGTAGTCTGTTTAGATTCCGTAGTTCGTGGGTATCAGTTTCGGTAGAGGTGCAGCATCGTGACACTTTTGCTAAC
AGGTACCACTTCTGATCACCTGTACATACATGAGCCGAAAGGCACAATCACTGTTTCAGATTTAAATTTATAGTGTGT
20 TTGTTTGGTCCAGAACTGAGACAATCACATGACAGTCAACGAGGAGAGAAAATTTAAAAATAAAAATAAAAACAAA
AAAAATTTAAAAATTAATAAATAAAGTCTAATAAGAACTTTGGTACAGGAACCTTTTTGTAAATATACATGTA
TGAATTGTTTCAGAGTTTATATTAATTTAATTGCTAAGCAAGAGACTAGGGACAGGCAAGATAATTTATGGC
AAAGTGTTTAAATTTATACATAAATAAAGTCTCTAAACTCCTGTG

The FCTR3f polypeptide (SEQ ID NO:13) encoded by SEQ ID NO:12 is 2724 amino
25 acid residues long and is presented using the one-letter code in Table 3I. This sequence
differs from FCTR3b in that it is missing amino acids 758-766 from that polypeptide.

Table 3I. Encoded FCTR3f protein sequence (SEQ ID NO:13)

MDVKDRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLTKAYDHDSRMHYGNRVTDLIHRESDEFPRQGTNFTLAE
LGICEPSPHRSGYCSDMGLLHQGYSLSTGSDADSDTEGGMSPEHAIRLWGRGIKSRSSGLSSRENSALTLTSDNENKSDDE
30 NGRPIPTTSSPSSLLPSAQLPSSHNPPVSCQMPLLDNNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHQSSTLR
PPLPPHNHTLSHHSSANSLNRRSLNRRSQIHAPAPAPNDLATTPEVQLQDSWVLSNVPLETRHFLFKTSSGSTPLFSS
SSPGYPLTSGTVTTPPPRLLPRNTFSRKAFLLKKPSKYCSWKCAALSAIAAALLAILLAYFIVPWSLKNSSIDSGEAEVGRR
VTQEVPPGVFWRSQIHISQPFLLFNISLKGDALFGVYIRRLGPPSHAQYDFMERLDGKEKWSVVEsprRRSIQTLVQNEAV
35 FQYLDVGLWHLAFYNDGDKEMVSEFTVVLDSVQDCPRNCHNGNECVSGVCHCFPGFLGADCAKAACPVLCSNGQYSKGT
QCYSWGKGAECVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEVDCLDPTCSSHGVCVNGECLSPGWGGLNCELARVQ
CPDQCSHGTYLPDTGLCSCDPNWMPDCSVEVCSVDGTHGVCIIGACRCEEGWGAACDQVCHPRCI EHGTCKDGKCECR
EGWNGEHTIDGCPDLNCGNRCRTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEGDGLVDCLDPDCCLOSAQNSLLCR
GSRDPLDI IQQGTQDWPVAVKSFYDIKLLAGKDSITHIIPGENPFSLSLVLIRGQVVTDDGTPLVGVNVSFVKYKGYTITR
40 QDGTFDLIANGGASLTLLHFERAPFMSQERTVWLPWNSFYAMDITLVMTKEENSIPSCDLSGFVRPDPII ISSPLSTFFSAAPGQ
NPVIVPETQVLHHEIELPGSNVKLRLYSSRTAGYKSLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKT
DAYGQVRVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELDPNLSLGGWSLDKHHILNVKSGILHKGTEGENQFLTQQPAIIT
SIMGNRRRSISPCSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRVNVSILELRNKEFKHSNNPAHKYVLAVDP
VSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVAVAGTEGQCLPFDEARCGDGGKAI DATLMSPRGIAVDKNGLMYFVDATMIR
45 KVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNLSYVLENNVILRITENHQVSI IAGRPMHCQVPGI
DYSLSKLAIHSALESASAIASHTGVLYITETDEKKINRLRQVTTNGEICLLAGAASDCDCNDVNCNCYSGDDAYATDAILN
SPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNVTE
LIDNNGNSLKIIRRDSSGMPRHLLMPDNQIITLTGVTNGGLKVSTQNLLEGLMTYDNGTGLLATKSDDETGWTTFYDYDHEGRL
TNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTVITNLSSVEASYTVQDQVRNSYQLCNGTLRVMYANGMGSIFHSEPH
50 VLAGTITPTIGRCNISLPMENGLNSIEWLRKEQIKGVTIIFGRKL RVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRIIYDQV
GRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERDIDKQGRIVSRMFADGKVWSYSYLDKSMVLLLSQSRQYIFEYDSSD
RLLAVTMPVSARHSMSTHTSIGYIRNIYNPPESNASVIFDYSDDGRIKTSFLGTGRQVFYKYGKLSKLSIIVYDSTAVTFGY
DETTGVLKMNVLQSGGFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHNSFRIASIKPVISETPLPVDLYRYDEISGK
VEHFGKFGVYIDINQIITTAVMTL SKHFDTHGRIKEVQYEMFRSLMYWMTVQYDSMGRVVKRELKLGYPANTTKYTYDYDGD
60 GQLQSVAVNDRPTWRYSDYDLNGLHLNPGNSVRLMRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRYN
KASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPRITHVYNHNSNEITSLYYDLQGLHFAMESSSGEEYVYASDNTGT
PLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVKGEPAPFNL
YMFKSNNPLSSELDLKNYVTDVKSWMVFGFQLSNII PGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNOAFMAL
EGQVITKKLHASIREKAGHWFATTTPIIGKIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTYFVK
IGSADGDLVTLGTTTGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFYQSTLLLSIRYGLTPDTLDEEKARVLDQARQALGT
AWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYVLPVEQYPELADSSSNIQFLRQNEMGKR

SBJCT: 1274 GCCATTTTGGCTGGCATATTCATAG 1298

SCORE = 480 BITS (242), EXPECT = E-132
IDENTITIES = 365/406 (89%)
STRAND = PLUS / PLUS

QUERY: 797 AGTGCCTGCTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 856

SBJCT: 1420 AGTGCCTGCTCATTGAAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479

QUERY: 857 GGTAACACAAGAAGTCCCACCAGGGGTGTTTGGAGGTACAAATTACATCAGTCAGCC 916

SBJCT: 1480 GGTGACACAGGAAGTCCCACCAGGGGTGTTTGGAGGTCCCAGATTACATCAGTCAGCC 1539

QUERY: 917 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTGGTGTTCATAAG 976

SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTGGGCAAGGATGCCCTCTCGGTGTCTATAAG 1599

QUERY: 977 AAGAGGACTTCCACCATCTCATGCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1036

SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659

QUERY: 1037 GAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGAGCATACAGACCTTGGTTCAGAA 1096

SBJCT: 1660 GAAATGGAGCGTGGTTCGAGTCCGCCAGGGAACGCCGAGCATCCAGACTCTGGTGCAGAA 1719

QUERY: 1097 TGAAGCCGTGTTTGTGTCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1156

SBJCT: 1720 CGAGGCTGTGTTTGTGTCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779

QUERY: 1157 TGGAAAAGACAAAGAGATGGTTTCCCTTCAATACTGTTGTCTTAGAT 1202

SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGAT 1825

SCORE = 125 BITS (63), EXPECT = 7E-26
IDENTITIES = 93/103 (90%)
STRAND = PLUS / PLUS

QUERY: 1258 GATTCAGTGCAGGACTGTCCACGTAAGTCCATGGGAATGGTGAATGTGTGTCGGGGTG 1317

SBJCT: 1823 GATTCAGTGCAGGACTGTCCACGGAAGTGTACGGGAACGGTGAATGCGTGTCTGGACTG 1882

QUERY: 1318 TGTCACTGTTTCCAGGATTCTAGGAGCAGACTGTGCTAAAG 1360

SBJCT: 1883 TGTCACTGTTTCCAGGATTCTAGGTGCAGACTGTGCTAAAG 1925

In another BLASTN search it was found that the FCTR3a nucleic acid has homology to three fragments of *Gallus gallus* mRNA for teneurin-2. It has 541 of 629 bases (86%) identical to bases 502-1130, 302 of 367 bases (82%) identical to bases 1330-1696, and 87 of 103 bases (84%) identical to bases 1711-1813 of *Gallus gallus* mRNA for teneurin-2 (EMBL Acc: AJ245711.1) (Table 3K).

Table 3K. BLASTN of FCTR3a against *Gallus gallus* mRNA for teneurin-2 (SEQ ID NO:63)

>GI|6010048|EMBL|AJ245711.1|GGA245711 GALLUS GALLUS MRNA FOR TENEURIN-2, SHORT
SPLICE VARIANT (TEN2 GENE)
LENGTH = 2496

SCORE = 549 BITS (277), EXPECT = E-153
 IDENTITIES = 541/629 (86%)
 STRAND = PLUS / PLUS

5 QUERY: 114 GGTCGTCCCATTCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGC 173
 SBJCT: 502 GGTCGTCCCATTCACCTACATCCTCGTCTAGCCTTCTCCCATCTGCTCAGCTGCCCAGT 561

10 QUERY: 174 TCCCATATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCAT 233
 SBJCT: 562 TCTCATATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCAT 621

15 QUERY: 234 CAAATCATGGACACCAACCTTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCA 293
 SBJCT: 622 CAAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTCATACCTACTAAGAGCA 681

20 QUERY: 294 TGCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACT 353
 SBJCT: 682 TGTTCAAGGGCCACAGCAGGCATCCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACG 741

25 QUERY: 414 AACTCCCTCAACAGGAACCTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCA 473
 SBJCT: 802 AACTCCCTCAACAGGAACCTCGCTCACCAACCGCGCAACCAGATCCACGCGCTGCTCCC 861

30 QUERY: 474 GCGCCCAATGACCTGGCCACCACACCAGAGTCCGTTTCAAGACCTCCTCGGGGAGCACA 533
 SBJCT: 862 GCTCCCAATGACCTGGCGACCACGCTGAGTCTGTGAGCTGCAGGACAGCTGGGTGCTC 921

35 QUERY: 534 AACAGCAACGTGCCACTGGAGACCCGGCACTTCTCTTCAAGACCTCCTCGGGGAGCACA 593
 SBJCT: 922 AACAGCAACGTGCCGTGGAGACCCGGCATTCTTGTGTTAAGACATCTTCTGGAACGACT 981

40 QUERY: 594 CCCTTGTTTCAGCAGCTCTTCCCCGGGATACCTTTGACCTCAGGAACGGTTTACACGCCC 653
 SBJCT: 982 CCGCTGTTTCAGTAGCTCTTCCCCGTGCTACCCACTGACCTCAGGAACAGTTTATACTCCA 1041

45 QUERY: 654 CCGCCCCGCTGTGCCCAGGAATACTTTCTCCAGGAAGGCTTTCAAGCTGAAGAAGCCC 713
 SBJCT: 1042 CCTCCCAGGCTGTACCTAGAAATACATTTTCCAGGAATGCATTCAAGCTGAAAAAGCCC 1101

50 QUERY: 714 TCCAAATACTGCAGCTGGAAATGTGCTGC 742
 SBJCT: 1102 TCCAAGTATTGTAGCTGGAAATGTGCTGC 1130

SCORE = 212 BITS (107), EXPECT = 4E-52
 IDENTITIES = 302/367 (82%)
 STRAND = PLUS / PLUS

55 QUERY: 819 AGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCGGGTAACACAAGAAGTCCCACCA 878
 SBJCT: 1330 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTACCCAAGAGGTGCCCCCT 1389

60 QUERY: 879 GGGGTGTTTTGGAGGTACAAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 938
 SBJCT: 1390 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCTGAAGTTCAACATA 1449

65 QUERY: 939 TCCCTCGGAAGGACGCTCTCTTTGGTGTGTTACATAAGAAGAGGACTTCCACCATCTCAT 998
 SBJCT: 1450 TCCCTAGGAAGGATGCTCTTTTCGGTGTGTTATATAAGAAGAGGACTCCCACCATCACAT 1509

QUERY: 999 GCCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCT 1058
 SBJCT: 1510 GCACAGTATGATTTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGAATCC 1569

QUERY: 3567 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 3626
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 301 TGGACTCTCAGATGCTGTTGTGTCTGTGCGGGTTTGAATATGAGACCTGTCCCAGTCTAAT 360

 5 QUERY: 3627 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 3686
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 361 TCTCTGGGAGAAAAGGACAGCCCTCCTTCAGGGATTCGAGCTGGACCCCTCCAACCTCGG 420

 10 QUERY: 3687 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 3746
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 421 TGGCTGGTCCCTAGACAAACACCACATCCTCAATGTTAAAAGTGGAATCCTACACAAAGG 480

 QUERY: 3747 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 3806
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 15 SBJCT: 481 CACTGGGGAAAACAGTTCCTGACCCAGCAGCCTGCCATCATCACCAGCATCATGGGCAA 540

 QUERY: 3807 TGGTCGCGCCCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 3866
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 20 SBJCT: 541 TGGTCGCGCCCGGAGCATTTCCTGTCCCAGCTGCAACGGCCTTGCTGAAGGCAACAAGCT 600

 QUERY: 3867 GCTGGCCCCAGTGGCTCTGGCTGTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 3926
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 601 GCTGGCCCCAGTGGCTCTGGCTGTGGAATCGATGGGAGCCTCTATGTGGGTGACTTCAA 660

 25 QUERY: 3927 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAA 3986
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 661 TTACATCCGACGCATCTTTCCCTCTCGAAATGTGACCAGCATCTTGAGTTACGAAATAA 720

 QUERY: 3987 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 4046
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 30 SBJCT: 721 AGAGTTTAAACATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTC 780

 QUERY: 4047 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 4106
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 35 SBJCT: 781 CGGCTCGCTCTACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAG 840

 QUERY: 4107 TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 4166
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 841 TGGAACCAAAGACCTGGCTGGGAATTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCT 900

 40 QUERY: 4167 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 4226
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 901 ACCCTTTGATGAAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAG 960

 45 QUERY: 4227 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTGCGATGCCACCATGAT 4286
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 961 CCCGAGAGGTATTGCAGTAGACAAGAATGGGCTCATGTACTTTGTGCGATGCCACCATGAT 1020

 QUERY: 4287 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 4346
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 50 SBJCT: 1021 CCGGAAGGTTGACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGC 1080

 QUERY: 4347 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGCTGGAGTGGCC 4406
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 55 SBJCT: 1081 CGTCCGGCCGCTGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGCTGGAGTGGCC 1140

 QUERY: 4407 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAACAAATGTCAT 4466
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1141 AACAGACCTTGCTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAACAAATGTCAT 1200

 60 QUERY: 4467 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 4526
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1201 CCTTCGAATCACCGAGAACCACCAAGTCAGCATCATTGCGGGACGCCCCATGCACTGCCA 1260

 65 QUERY: 4527 AGTTCCTGGCATTGACTACTCACTCAGCAAAC TAGCCATTCACTCTGCCCTGGAGTCAGC 4586
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1261 AGTTCCTGGCATTGACTACTCACTCAGCAAAC TAGCCATTCACTCTGCCCTGGAGTCAGC 1320

QUERY: 4587 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 4646
 SBJCT: 1321 CAGTGCCATTGCCATTTCTCACACTGGGGTCCTCTACATCACTGAGACAGATGAGAAGAA 1380
 5 QUERY: 4647 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 4706
 SBJCT: 1381 GATTAACCGTCTACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGC 1440
 10 QUERY: 4707 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTAGGAGATGATGCCTA 4766
 SBJCT: 1441 CTCGGACTGCGACTGCAAAAACGATGTCAATTGCAACTGCTATTAGGAGATGATGCCTA 1500
 QUERY: 4767 CGCGACTGATGCCATCTTGAATTCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 4826
 15 SBJCT: 1501 CGCGACTGATGCCATCTTGAATTCCCATCATCCTTAGCTGTAGCTCCAGATGGTACCAT 1560
 QUERY: 4827 TTACATTGCAGACCTTGGAATATTTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 4886
 SBJCT: 1561 TTACATTGCAGACCTTGGAATATTTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCT 1620
 20 QUERY: 4887 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCGGAGAGCAGGAGTTATATGTTTCAA 4946
 SBJCT: 1621 TAATGCCTTCAACCAGTATGAGGCTGCATCCCCGGAGAGCAGGAGTTATATGTTTCAA 1680
 25 QUERY: 4947 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 5006
 SBJCT: 1681 CGCTGATGGCATCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTT 1740
 30 QUERY: 5007 CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCTGAA 5066
 SBJCT: 1741 CACATATAGTACTGACAATGATGTCACTGAATTGATTGACAATAATGGGAATTCCTGAA 1800
 QUERY: 5067 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 5126
 35 SBJCT: 1801 GATCCGTCGGGACAGCAGTGGCATGCCCCGTACCTGCTCATGCCTGACAACCAGATCAT 1860
 QUERY: 5127 CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT 5186
 SBJCT: 1861 CACCCTCACCGTGGGCACCAATGGAGGCCTCAAAGTCGTGTCCACACAGAACCTGGAGCT 1920
 40 QUERY: 5187 TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG 5246
 SBJCT: 1921 TGGTCTCATGACCTATGATGGCAACACTGGGCTCCTGGCCACCAAGAGCGATGAAACAGG 1980
 45 QUERY: 5247 ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTGACGCGCCCCAC 5306
 SBJCT: 1981 ATGGACGACTTTCTATGACTATGACCACGAAGGCCGCTGACCAACGTGACGCGCCCCAC 2040
 50 QUERY: 5307 GGGGGTGGTAACCACTCTGCACCGGAAATGGAGAAATCTATTACCATTGACATTGAGAA 5366
 SBJCT: 2041 GGGGGTGGTAACCACTCTGCACCGGAAATGGAGAAATCTATTACCATTGACATTGAGAA 2100
 QUERY: 5367 CTCCAACCGTGATGATGACGTCACTGTATCACCACCTCTCTTCAGTAGAGGCCTCCTA 5426
 55 SBJCT: 2101 CTCCAACCGTGATGATGACGTCACTGTATCACCACCTCTCTTCAGTAGAGGCCTCCTA 2160
 QUERY: 5427 CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG 5486
 SBJCT: 2161 CACAGTGGTACAAGATCAAGTTCGGAACAGCTACCAGCTCTGTAATAATGGTACCCTGAG 2220
 60 QUERY: 5487 GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCTAGCGGG 5546
 SBJCT: 2221 GGTGATGTATGCTAATGGGATGGGTATCAGCTTCCACAGCGAGCCCCATGTCTAGCGGG 2280
 65 QUERY: 5547 CACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAA 5606
 SBJCT: 2281 CACCATCACCCCCACCATTTGGACGCTGCAACATCTCCCTGCCTATGGAGAATGGCTTAA 2340

QUERY: 5607 CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG 5666
 SBJCT: 2341 CTCCATTGAGTGGCGCCTAAGAAAGGAACAGATTAAAGGCAAAGTCACCATCTTTGGCAG 2400
 5 QUERY: 5667 GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCATTGACTATGATCGAAATATTCGGAC 5726
 SBJCT: 2401 GAAGCTCCGGGTCCATGGAAGAAATCTCTTGTCATTGACTATGATCGAAATATTCGGAC 2460
 10 QUERY: 5727 TGAAAAGATCTATGATGACCACCGGAAGTTCACCTGAGGATCATTTATGACCAGGTGGG 5786
 SBJCT: 2461 TGAAAAGATCTATGATGACCACCGGAAGTTCACCTGAGGATCATTTATGACCAGGTGGG 2520
 15 QUERY: 5787 CCGCCCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT 5846
 SBJCT: 2521 CCGCCCCCTTCCTCTGGCTGCCCAGCAGCGGGCTGGCAGCTGTCAACGTGTCATACTTCTT 2580
 20 QUERY: 5847 CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA 5906
 SBJCT: 2581 CAATGGGCGCCTGGCTGGGCTTCAGCGTGGGGCCATGAGCGAGAGGACAGACATCGACAA 2640
 25 QUERY: 5907 GCAAGGCCGCATCGTGTCCCGCATGTTGCTGACGGGAAAGTGTGGAGTACTCCTACCT 5966
 SBJCT: 2641 GCAAGGCCGCATCGTGTCCCGCATGTTGCTGACGGGAAAGTGTGGAGTACTCCTACCT 2700
 30 QUERY: 5967 TGACAAGTCCATGGTCTCTCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC 6026
 SBJCT: 2701 TGACAAGTCCATGGTCTCTCTGCTTCAGAGCCAACGTCAGTATATATTTGAGTATGACTC 2760
 35 QUERY: 6027 CTCTGACCGCCTCCTTGCCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACA 6086
 SBJCT: 2761 CTCTGACCGCCTCCTTGCCGTCACCATGCCAGCGTGGCCCGGCACAGCATGTCCACACA 2820
 40 QUERY: 6087 CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCGGTCAT 6146
 SBJCT: 2821 CACCTCCATCGGCTACATCCGTAATATTTACAACCCGCTGAAAGCAATGCTTCGGTCAT 2880
 45 QUERY: 6147 CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA 6206
 SBJCT: 2881 CTTTGACTACAGTGATGACGGCCGCATCCTGAAGACCTCCTTTTTGGGCACCGGACGCCA 2940
 50 QUERY: 6207 GGTGTTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 6266
 SBJCT: 2941 GGTGTTTCTACAAGTATGGGAAACTCTCCAAGTTATCAGAGATTGTCTACGACAGTACCGC 3000
 55 QUERY: 6267 CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 6326
 SBJCT: 3001 CGTCACCTTCGGGTATGACGAGACCACTGGTGTCTTGAAGATGGTCAACCTCCAAAGTGG 3060
 60 QUERY: 6327 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 6386
 SBJCT: 3061 GGGCTTCTCCTGCACCATCAGGTACCGGAAGATTGGCCCCCTGGTGGACAAGCAGATCTA 3120
 65 QUERY: 6387 CAGGTTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 6446
 SBJCT: 3121 CAGGTTTCTCCGAGGAAGGCATGGTCAATGCCAGGTTTGACTACACCTATCATGACAACAG 3180
 QUERY: 6447 CTTCCGCATCGAAGCATCAAGCCCGTCATAAGTGAGACTCCCCCTCCCCGTTGACCTCTA 6506
 SBJCT: 3181 CTTCCGCATCGAAGCATCAAGCCCGTCATAAGTGAGACTCCCCCTCCCCGTTGACCTCTA 3240
 QUERY: 6507 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 6566
 SBJCT: 3241 CCGCTATGATGAGATTTCTGGCAAGGTGGAACACTTTGGTAAGTTTGGAGTCATCTATTA 3300
 QUERY: 6567 TGACATCAACCAGATCATCACCCTGCGGTGATGACCCTCAGCAAACACTTCGACACCCA 6626
 SBJCT: 3301 TGACATCAACCAGATCATCACCCTGCGGTGATGACCCTCAGCAAACACTTCGACACCCA 3360

QUERY:	6627	TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT	6686
SBJCT:	3361	TGGGCGGATCAAGGAGGTCCAGTATGAGATGTTCCGGTCCCTCATGTACTGGATGACGGT	3420
QUERY:	6687	GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAA	6746
SBJCT:	3421	GCAATATGACAGCATGGGCAGGGTGATCAAGAGGGAGCTAAAACTGGGGCCCTATGCCAA	3480
QUERY:	6747	TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA	6806
SBJCT:	3481	TACCACGAAGTACACCTATGACTACGATGGGGACGGGCAGCTCCAGAGCGTGGCCGTCAA	3540
QUERY:	6807	TGACCGCCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC	6866
SBJCT:	3541	TGACCGCCCCGACCTGGCGCTACAGCTATGACCTTAATGGGAATCTCCACTTACTGAACCC	3600
QUERY:	6867	AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT	6926
SBJCT:	3601	AGGCAACAGTGTGCGCCTCATGCCCTTGCGCTATGACCTCCGGGATCGGATAACCAGACT	3660
QUERY:	6927	CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT	6986
SBJCT:	3661	CGGGGATGTGCAGTACAAAATTGACGACGATGGCTATCTGTGCCAGAGAGGGTCTGACAT	3720
QUERY:	6987	CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGTGGAG	7046
SBJCT:	3721	CTTCGAATACAATTCCAAGGGCCTCCTAACAAGAGCCTACAACAAGGCCAGCGGTGGAG	3780
QUERY:	7047	TGTCCAGTACCCTATGATGGCGTAGGACGGCGGGCTTCTTACAAGACCAACCTGGGCCA	7106
SBJCT:	3781	TGTCCAGTACCCTATGATGGCGTAGGACGGCGGGCTTCTTACAAGACCAACCTGGGCCA	3840
QUERY:	7107	CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA	7166
SBJCT:	3841	CCACCTGCAGTACTTCTACTCTGACCTCCACAACCCGACGCGCATCACCCATGTCTACAA	3900
QUERY:	7167	TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT	7226
SBJCT:	3901	TCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCACCTCTTTGCCAT	3960
QUERY:	7227	GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC	7286
SBJCT:	3961	GGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGGACTCCTCTGGC	4020
QUERY:	7287	TGTGTTTCAAGCATCAACGGCCTCATGATCAAAACAGCTGCAGTACACGGCCTATGGGGAGAT	7346
SBJCT:	4021	TGTGTTTCAAGCATCAACGGCCTCATGATCAAAACAGCTGCAGTACACGGCCTATGGGGAGAT	4080
QUERY:	7347	TTATTATGACTCCAACCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA	7406
SBJCT:	4081	TTATTATGACTCCAACCCGACTTCCAGATGGTCATTGGCTTCCATGGGGGACTCTATGA	4140
QUERY:	7407	CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG	7466
SBJCT:	4141	CCCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTGGCAGGACGATG	4200
QUERY:	7467	GACCTCCCAGACTATACCATGTGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT	7526
SBJCT:	4201	GACCTCCCAGACTATACCATGTGAAAAACGTGGGCAAGGAGCCGGCCCCCTTTAACCT	4260
QUERY:	7527	GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC	7586
SBJCT:	4261	GTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTTGAAGAACTACGTGAC	4320
QUERY:	7587	AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT	7646
SBJCT:	4321	AGATGTGAAAAGCTGGCTTGTGATGTTTGGATTTCAGCTTAGCAACATCATTCCTGGCTT	4380

QUERY: 7647 CCCGAGAGCCAAAATGTATTTCTGTCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG 7706
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4381 CCCGAGAGCCAAAATGTATTTCTGTCCTCCTCCCTATGAATTGTCAGAGAGTCAAGCAAG 4440

 5 QUERY: 7707 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 7766
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4441 TGAGAATGGACAGCTCATTACAGGTGTCCAACAGACAACAGAGAGACATAACCAGGCCTT 4500

 10 QUERY: 7767 CATGGCTCTGGAAGGACAGGTCTATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 7826
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4501 CATGGCTCTGGAAGGACAGGTCTATTACTAAAAAGCTCCACGCCAGCATCCGAGAGAAAGC 4560

 QUERY: 7827 AGGTCACTGGTTTGCCACCACCACGCCCATCATTGGCAAAGGCATCATGTTTGCCATCAA 7886
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 15 SBJCT: 4561 AGGTCACTGGTTTGCCACCACCACGCCCATCATTGGCAAAGGCATCATGTTTGCCATCAA 4620

 QUERY: 7887 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 7946
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 20 SBJCT: 4621 AGAAGGGCGGGTGACCACGGGCGTGTCCAGCATCGCCAGCGAAGATAGCCGCAAGGTGGC 4680

 QUERY: 7947 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 8006
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4681 ATCTGTGCTGAACAACGCCTACTACCTGGACAAGATGCACTACAGCATCGAGGGCAAGGA 4740

 25 QUERY: 8007 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 8066
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4741 CACCCACTACTTTGTGAAGATTGGCTCAGCCGATGGCGACCTGGTCACACTAGGCACCAC 4800

 QUERY: 8067 CATCGGCCGCAAGGTGCTAGAGAGCGGGTGAACGTGACCGTGTCCAGCCACGCTGCT 8126
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 30 SBJCT: 4801 CATCGGCCGCAAGGTGCTAGAGAGCGGGTGAACGTGACCGTGTCCAGCCACGCTGCT 4860

 QUERY: 8127 GGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCAGTACTCCACGCTGTGCT 8186
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 35 SBJCT: 4861 GGTCAACGGCAGGACTCGAAGGTTACGAACATTGAGTTCAGTACTCCACGCTGTGCT 4920

 QUERY: 8187 CAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGAAGAGAAGGCCCGCTCCTGGA 8246
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 40 SBJCT: 4921 CAGCATCCGCTATGGCCTCACCCCCGACACCCTGGACGAAGAGAAGGCCCGCTCCTGGA 4980

 QUERY: 8247 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 8306
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 4981 CCAGGCGAGACAGAGGGCCCTGGGCACGGCCTGGGCCAAGGAGCAGCAGAAAGCCAGGGA 5040

 45 QUERY: 8307 CGGGAGAGAGGGGAGCCGCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 8366
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 5041 CGGGAGAGAGGGGAGCCGCTGTGGACTGAGGGCGAGAAGCAGCAGCTTCTGAGCACCGG 5100

 QUERY: 8367 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGAGCAATACCCAGAGCTTGC 8426
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 50 SBJCT: 5101 GCGCGTGCAAGGGTACGAGGGATATTACGTGCTTCCCGTGAGCAATACCCAGAGCTTGC 5160

 QUERY: 8427 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 8486
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 55 SBJCT: 5161 AGACAGTAGCAGCAACATCCAGTTTTTAAGACAGAATGAGATGGGAAAGAGGTAACAAAA 5220

 QUERY: 8487 TAATCTGCTGCCATTCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCCTCTCCT 8546
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 60 SBJCT: 5221 TAATCTGCTGCCATTCTTGTCTGAATGGCTCAGCAGGAGTAAGTGTATCTCCTCTCCT 5280

 QUERY: 8547 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 8606
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 5281 AAGGAGATGAAGACCTAACAGGGGCACTGCGGCTGGGCTGCTTTAGGAGACCAAGTGGCA 5340

 65 QUERY: 8607 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCTG 8666
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 5341 AGAAAGCTCACATTTTTTGAGTTCAAATGCTACTGTCCAAGCGAGAAGTCCCTCATCTG 5400

QUERY: 9651 GTCTAATAAGAACTTTGGTACAGGAACCTTTTTGTAATATACATGTATGAATTGTTTCATC 9710
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 6385 GTCTAATAAGAACTTTGGTACAGGAACCTTTTTGTAATATACATGTATGAATTGTTTCATC 6444

 5 QUERY: 9711 GAGTTTTTATATTAATTTAATTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 9770
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 6445 GAGTTTTTATATTAATTTAATTGCTGCTAAGCAAAGACTAGGGACAGGCAAAGATAAT 6504

 10 QUERY: 9771 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACCTCCTGTG 9826
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 6505 TTATGGCAAAGTGTTTAAATTGTTTATACATAAATAAAGTCTCTAAAACCTCCTGTG 6560

In this search it was also found that the FCTR3bcd and e nucleic acids had homology to five fragments of *Mus musculus* mRNA for Ten-m2. It has 5498 of 6108 bases (90%) identical to bases 2504-8610, 1095 of 1196 bases (91%) identical to bases 103-1298, 1000 of 1088 bases (91%) identical to bases 1420-2540, 81 of 89 bases (91%) identical to bases 8655-8743, and 30 of 32 bases (93%) identical to bases 7-38 of *Mus musculus* mRNA for Ten-m2 (Table 3M).

Table 3M. BLASTN of FCTR3b, c, d, and e against *Mus musculus* mRNA for Ten-m2
Mrna (SEQ ID NO:65)

>GI|4760777|DBJ|AB025411.1|AB025411 MUS MUSCULUS MRNA FOR TEN-M2, COMPLETE CDS
 LENGTH = 8797

 SCORE = 7263 BITS (3664), EXPECT = 0.0
 IDENTITIES = 5498/6108 (90%), GAPS = 1/6108 (0%)
 STRAND = PLUS / PLUS

 QUERY: 2578 GATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2637
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 30 SBJCT: 2504 GATGGCTGCCCTGATTGTGCAACGGTAACGGGAGATGCACACTGGGTGAGAACAGCTGG 2563

 QUERY: 2638 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCCATGGAAACTTCC 2697
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2564 CAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCTGGATGCAACGTTGCCATGGAAACTTCC 2623

 35 QUERY: 2698 TGTGCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGATTGTTTGGACCCTGACTGC 2757
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2624 TGCCTGATAACAAGGATAATGAGGGAGATGGCCTGGTGGACTGCTGGACCCTGACTGC 2683

 40 QUERY: 2758 TGCCTGCAGTCAGCCTGTGCAACAGCCTGCTCTGCCGGGGGTCCCGGGACCCACTGGAC 2817
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2684 TGCCTACAGTCAGCCTGTGCAACAGCCTGCTCTGCCGGGGGTCTCGGGACCCCTTGGAC 2743

 45 QUERY: 2818 ATCATTACAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTATGACCGTATCAAG 2877
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2744 ATCATTACAGCAAGGTCAGACAGACTGGCCTGAGTGAAGTCCTTCTATGACCGCATCAAG 2803

 QUERY: 2878 CTCTTGGCAGGCAAGGATAGCAACCCACATCATTCTGGAGAGAACCCTTTCAACAGCAGC 2937
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 50 SBJCT: 2804 CTCTTGGCAGGCAAGGACAGCAACCCACATCATTCTGGAGACAACCCCTTCAATAGCAGC 2863

 QUERY: 2938 TTGGTTTCTCTCATCCGAGGCCAAGTAGTAACACAGATGGAACCTCCCTGGTGGTGTG 2997
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2864 CTGGTGTCTCTGATCCGAGGCCAAGTAGTAACCATGGATGGGACTCCCTTGGTGGTGTG 2923

 55 QUERY: 2998 AACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGCCAGGATGGCAGC 3057
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 2924 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGATGGCAGC 2983

[illegible]

QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAAACCAAAGACCTGGCTGGGAATTCGGAA 4137
 SBJCT: 4004 CGCCGAATCTACCGAGTCAAGTCTCTGAGCGGAGCCAAAGACCTGGCTGGAAATTCGGAA 4063
 5
 QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCCTTGATGAAGCCCGCTGCGGGGATGGA 4197
 SBJCT: 4064 GTTGTGGCAGGGACTGGCGAACAATGTCTACCCCTTGATGAAGCCCGCTGTGGGGATGGA 4123
 10
 QUERY: 4198 GGGAAAGCCATAGATGCAACCCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257
 SBJCT: 4124 GGGAAAGCTGTGGACGCCACCCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4183
 15
 QUERY: 4258 CTCATGTACTTTGTTCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317
 SBJCT: 4184 CTTATGTACTTTGTTGATGCCACCATGATCCGGAAGGTGGACCAAACGGAATCATCTCC 4243
 20
 QUERY: 4318 ACCCTGCTGGGCTCCAATGACCTCACTGCCGCTCCGCGCGCTGAGCTGTGATTCCAGCATG 4377
 SBJCT: 4244 ACCCTGCTGGGCTCCAATGACCTCACAGCTGTCCGACCACTGAGCTGTGACTCGAGCATG 4303
 25
 QUERY: 4378 GATGTAGCCCAGGTTCTGCTGAGTGGCCAAACAGACCTTGCTGTCAATCCCATGGATAAC 4437
 SBJCT: 4304 GACGTGGCCAGGTCCGTCTAGAATGGCCGACAGACCTCGCCGCTCAACCCCATGGACAAC 4363
 30
 QUERY: 4438 TCCTTGATGTCTTAGAGAACAATGTCATCCTTCGAATCACCAGAGAACCACCAAGTCAGC 4497
 SBJCT: 4364 TCCCTGTACGTTCTGGAGAACAACGTCATCCTGCGGATCACGGAGAACCACCAAGTCAGC 4423
 35
 QUERY: 4498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAAA 4557
 SBJCT: 4424 ATCATCGCGGGACGGCCTATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAA 4483
 40
 QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617
 SBJCT: 4484 CTCGCCATCCACTCTGCGCTGGAATCAGCCAGCGCCATTGCCATTTCTCACACTGGGGTG 4543
 45
 QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677
 SBJCT: 4544 CTCTACATCACTGAGACGAGACGAGAAGAAGATCAACCGCCTACGCCAAGTCACCACCAAT 4603
 50
 QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737
 SBJCT: 4604 GGAGAGATCTGCCTCTTAGCCGGGGCGGCTCAGACTGTGACTGCAAAAACGATGTCAAC 4663
 55
 QUERY: 4738 TGCAACTGCTATTTCAGGAGATGATGCTACGCGACTGATGCCATCTTGAATTCCCCATCA 4797
 SBJCT: 4664 TGCATCTGCTACTCGGGAGATGACGCTTACGCCACGACGCCATCCTGAACTCGCCGTCC 4723
 60
 QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAAATATTCGGATC 4857
 SBJCT: 4724 TCCTTAGCCGTGGCTCCGGATGGCACCATCTACATTGCAGACCTTGGGAATATCCGGATC 4783
 65
 QUERY: 4858 AGGGCGGTCTAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917
 SBJCT: 4784 AGGGCGGTCTAGCAAAAATAAACCCGTCTTAACGCATTCAACCAGTATGAGGCTGCATCT 4843
 QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977
 SBJCT: 4844 CCGGGAGAACAGGAATTGTACGTGTTCAACGCTGATGGTATCCATCAGTACACTGTGAGT 4903
 QUERY: 4978 CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAA 5037
 SBJCT: 4904 CTGGTGACTGGGGAGTACTTGTACAATTTACATACAGCGCTGACAATGACGTACCGGAG 4963
 QUERY: 5038 TTGATTGACAATAATGGGAATTCCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCGCT 5097
 SBJCT: 4964 TTGATTGACAACAACGGGAATTCCCTAAAGATCCGCCGGGACAGCAGTGGCATGCCCGGC 5023

QUERY: 5098 CACCTGCTCATGCCTGACAACCAGATCATCACCTCACCGTGGGCACCAATGGAGGCCTC 5157
 |||||
 SBJCT: 5024 CACCTGCTCATGCCGATAATCAGATTATCACCTTACTGTGGGCACCAATGGAGGCCTC 5083
 5
 QUERY: 5158 AAAGTCGTGTCCACACAGAACCCTGGAGCTTGGTCTCATGACCTATGATGGCAACACTGGG 5217
 |||||
 SBJCT: 5084 AAAGCCGTGTCCACTCAGAACCCTGGAGCTGGGCCTCATGACTTATGATGGGAACACTGGA 5143
 10
 QUERY: 5218 CTCCTGGCCACCAAGAGCGATGAAACAGGATGGACGACTTTCTATGACTATGACCACGAA 5277
 |||||
 SBJCT: 5144 CTCCTAGCCACCAAGAGTGATGAAACCGGATGGACAACCTTTTATGACTATGACCACGAG 5203
 15
 QUERY: 5278 GGCCGCTGACCAACGTGACGCGCCCCACGGGGTGGTAACCAGTCTGCACCGGAAATG 5337
 |||||
 SBJCT: 5204 GGCCGTCTGACCAATGTGACCCGCCCCACGGGCGTGGTGACCAGTCTGCACCGGAAATG 5263
 20
 QUERY: 5338 GAGAAATCTATTACCATTGACATTGAGAACTCCAACCGTGATGATGACGTCACTGTCTATC 5397
 |||||
 SBJCT: 5264 GAGAAATCTATCACCATTGACATTGAGAACTCCAACCGGGATGATGACGTCACTGTGATC 5323
 25
 QUERY: 5398 ACCAACCTCTCTTCAGTAGAGGCCTCTACACAGTGGTACAAGATCAAGTTCGGAACAGC 5457
 |||||
 SBJCT: 5324 ACCAACCTCTCTCCGTGGAGGCCTCTATACAGTGGTACAAGATCAAGTTCGGAACAGC 5383
 30
 QUERY: 5458 TACCAGCTCTGTAATAATGGTACCCTGAGGGTGATGTATGCTAATGGGATGGGTATCAGC 5517
 |||||
 SBJCT: 5384 TACCAGCTCTGCAATAATGGAACCTGCGGGTGATGTACGCCAACGGCATGGCTGTCAGC 5443
 35
 QUERY: 5518 TTCCACAGCGAGCCCCATGTCCTAGCGGGCACCATCACCCCCACCATTGGACGCTGCAAC 5577
 |||||
 SBJCT: 5444 TTCCACAGTGAGCCCCACGTCTCGCAGGCACCATCACCCCCACCATCGGGCGCTGCAAC 5503
 40
 QUERY: 5578 ATCTCCCTGCCTATGGAGAATGGCTTAAACTCCATTGAGTGGCGCCTAAGAAAGGAACAG 5637
 |||||
 SBJCT: 5504 ATCTCTCTGCCCATGGAGAATGGCTTGAACCTCATCGAGTGGCGCCTGAGGAAGGAACAG 5563
 45
 QUERY: 5638 ATTAAAGGCAAAGTCACCATCTTTGGCAGGAAGCTCCGGGTCCATGGAAGAAATCTCTTG 5697
 |||||
 SBJCT: 5564 ATCAAAGGCAAAGTCACCATCTTTGGGAGGAAGCTTCGGGTCCACGGAAGGAATCTCTTG 5623
 50
 QUERY: 5698 TCCATTGACTATGATCGAAATATTCGGAAGTCTATGATGACCACCGGAAGTTC 5757
 |||||
 SBJCT: 5624 TCCATTGATTATGACCGAAATATCCGTACGGAGAAGATCTACGATGACCACCGGAATTC 5683
 55
 QUERY: 5758 ACCCTGAGGATCATTTATGACCAGGTGGGCGCCCCCTTCTCTGGCTGCCAGCAGCGGG 5817
 |||||
 SBJCT: 5684 ACCCTGAGGATCATCTATGACCAGGTGGGCGCCCCCTTCTGTGGCTCCCGAGCAGTGGG 5743
 60
 QUERY: 5818 CTGGCAGCTGTCAACGTGTCTACTTCTTCAATGGGCGCCTGGCTGGGCTTCAGCGTGGG 5877
 |||||
 SBJCT: 5744 CTGGCAGCCGTCAATGTCTCTACTTCTTCAATGGGCGCTTGGCCGGCCTCCAGCGAGGG 5803
 65
 QUERY: 5878 GCCATGAGCGAGAGGACAGACATCGACAAGCAAGGCCGATCGTGTCCCGCATGTTTCGCT 5937
 |||||
 SBJCT: 5804 GCCATGAGCGAGAGGACAGACATTGACAAGCAAGGCCGATCGTGTCCCGCATGTTTCGCC 5863
 QUERY: 5938 GACGGGAAAGTGTGGAGCTACTCCTACCTTGACAAGTCCATGGTCTCTGCTTCAGAGC 5997
 |||||
 SBJCT: 5864 GACGGGAAAGTCTGGAGTTATCTCTATCTTGACAAGTCCATGGTCTCTGCTACAGAGC 5923
 QUERY: 5998 CAACGTCACTATATATTTGAGTATGACTCCTCTGACCGCCTCCTTGCCGTCAACATGCCC 6057
 |||||
 SBJCT: 5924 CAACGTCACTATATTTGAATATGACTCCTCCGATCGCTCCACGCAGTCACTATGCCC 5983
 QUERY: 6058 AGCGTGGCCCGGCACAGCATGTCCACACACCTCCATCGGCTACATCCGTAATATTAC 6117
 |||||
 SBJCT: 5984 AGTGTGCGCCCGGCACAGCATGTCCACGCACCTCCATTGGTTACATCCGAAACATTAC 6043

QUERY: 6118 AACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG 6177
 SBJCT: 6044 AACCCACCCGAAAGCAATGCATCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTA 6103
 5
 QUERY: 6178 AAGACCTCCTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG 6237
 SBJCT: 6104 AAGACATCTTTCTTGGGCACTGGGCGCCAGGTGTTCTACAAGTATGGGAAACTCTCCAAG 6163
 10
 QUERY: 6238 TTATCAGAGATTGTCTACGACAGTACCGCCGTACCTTCGGGTATGACGAGACCACTGGT 6297
 SBJCT: 6164 TTATCAGAGATAGTCTACGACAGCAGCCGTACCTTCGGGTATGACGAGACCACTGGT 6223
 15
 QUERY: 6298 GTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCTGCACCATCAGGTACCGGAAG 6357
 SBJCT: 6224 GTCTTGAAGATGGTCAATCTCCAAAGTGGGGGCTTCTCTGTACCATCAGGTACCGAAAG 6283
 20
 QUERY: 6358 ATTGGCCCCCTGGTGGACAAGCAGATCTACAGGTTCTCCGAGGAAGGCATGGTCAATGCC 6417
 SBJCT: 6284 GTTGGGGCCCTTGTGGACAAGCAGATTACAGGTTCTCTGAGGAAGGAATGATCAACGCC 6343
 25
 QUERY: 6418 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCGTCATA 6477
 SBJCT: 6344 AGGTTTGATTATACCTATCAGACAATAGCTTCCGCATGCCAGCATCAAAACCCGTCATT 6403
 30
 QUERY: 6478 AGTGAGACTCCCCCTCCCCGTGACCTCTACCGCTATGATGAGATTTCTGGCAAGGTGGAA 6537
 SBJCT: 6404 AGCGAGACTCCCCTTCTGTGACCTCTACCGCTATGACGAGATTTCCGCAAGGTGGAA 6463
 35
 QUERY: 6538 CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCCTGCCGTG 6597
 SBJCT: 6464 CACTTCGGCAAGTTTGGGGTCATCTACTACGACATCAACCAGATCATCACCCTGCCGTG 6523
 40
 QUERY: 6598 ATGACCTCAGCAAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG 6657
 SBJCT: 6524 ATGACGCTTAGCAAGCACTTTGACACCCATGGGCGCATCAAGGAAGTGAATATGAGATG 6583
 45
 QUERY: 6658 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG 6717
 SBJCT: 6584 TTCCGGTCCCTCATGTACTGGATGACTGTGCAATATGACAGTATGGGTAGGGTCATCAAG 6643
 50
 QUERY: 6718 AGGGAGCTAAAACTGGGGCCCTATGCCAATACCACGAAGTACACCTATGACTACGATGGG 6777
 SBJCT: 6644 AGGGAACTGAAACTAGGGCCCTATGCCAACCACCAAAGTACACCTATGACTATGACGGG 6703
 55
 QUERY: 6778 GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC 6837
 SBJCT: 6704 GACGGGCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGCTATAGCTATGAC 6763
 60
 QUERY: 6838 CTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC 6897
 SBJCT: 6764 CTCAATGGGAACCTGCACCTTCTAAACCCAGGAAACAGTGCTGCGCCTCATGCCCTTACGC 6823
 65
 QUERY: 6898 TATGACCTCCGGGATCGGATAACCAGACTCGGGGATGTGAGTACAAAATTGACGACGAT 6957
 SBJCT: 6824 TATGACCTCCGTGACCGGATAACCAGGCTAGGGGACGTGAGTACAAAATCGATGACGAT 6883
 QUERY: 6958 GGCTATCTGTGCCAGAGAGGGTCTGACATCTTGAATACAATCCAAGGGCCTCCTAACA 7017
 SBJCT: 6884 GGCTATTTGTGCCAGAGAGGGTCTGACATCTTGAATACAACCTCCAAGGGCCTTCTGACG 6943
 QUERY: 7018 AGAGCCTACAACAAGGCCAGCGGTGGAGTGTCAGTACCGCTATGATGGCGTAGGACGG 7077
 SBJCT: 6944 AGAGCATACAACAAGGCCAGCGGATGGAGCGTGAGTACCGCTATGACGGAGTGGCCGC 7003
 QUERY: 7078 CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC 7137
 SBJCT: 7004 CGGGCTTCCTACAAGACCAACCTGGGCCACCACCTACAGTACTTCTACTCCGACCTCCAC 7063

5
 QUERY: 7138 AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTAC 7197
 SBJCT: 7064 AACCCACACGTATCACCCATGTTTACAACCACTCCAACCTCTGAGATCACCTCGCTCTAC 7123
 10
 QUERY: 7198 TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT 7257
 SBJCT: 7124 TATGACCTCCAGGGCCACCTATTTGCCATGGAGAGCAGTAGTGGTGAAGAATACTATGTC 7183
 15
 QUERY: 7258 GCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTTACGATCAACGGCCTCATGATCAAA 7317
 SBJCT: 7184 GCCTCAGACAACACGGGGACCCCTCTGGCTGTGTACAGTATCAATGGCCTCATGATCAAG 7243
 20
 QUERY: 7318 CAGCTGCAGTACACGGCCTATGGGGAGATTTATTATGACTCCAACCCGACTTCCAGATG 7377
 SBJCT: 7244 CAAGCTGCAGTACACAGCCTATGGGGAGATCTACTATGACTCCAATCCAGACTTCCAGATG 7303
 25
 QUERY: 7378 GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAG 7437
 SBJCT: 7304 GTCATTGGCTTCCACGGAGGCTCTATGACCCCTCACCAGCTCGTCCACTTTACTCAA 7363
 30
 QUERY: 7438 CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497
 SBJCT: 7364 CGTGATTATGACGTGCTGGCAGGACGCTGGACGTCCCCGACTACACCATGTGGAGGAAC 7423
 35
 QUERY: 7498 GTGGGCAAGGAGCCGGCCCCCTTTAACTGTATATGTTCAAGAGCAACAATCCTCTCAGC 7557
 SBJCT: 7424 GTGGGCAAGGAGCCAGCCCCCTTCAACTGTACATGTTCAAGAACAACAATCCTCTGAGC 7483
 40
 QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGA 7617
 SBJCT: 7484 AATGAGCTGGAATTTAAAGAACTACGTGACAGAGCTGAAGAGCTGGCTTGTGATGTTTGA 7543
 45
 QUERY: 7618 TTTCAGCTTAGCAACATCATTCTGGCTTCCCGAGAGCCAAATGTATTTCTGTCCTCCT 7677
 SBJCT: 7544 TTTCAGCTCAGCAACATCATTCTGGATTCCCGAGAGCCAAATGTATTTTGTGCTCCC 7603
 50
 QUERY: 7678 CCCTATGAATTGTGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA 7737
 SBJCT: 7604 CCCTATGAAGTGTGAGAGTCAAGCAAGCGAGAACGGACAGCTCATTACAGGTGTCCAG 7663
 55
 QUERY: 7738 CAGACAACAGAGAGACATAACCAGGCTTTCATGGCTCTGGAAGGACAGGTCATTACTAAA 7797
 SBJCT: 7664 CAGACAAGTGAAGGCATACCAGGCTTCTGGCTCTGGAAGGACAGGTCATCACTAAA 7723
 60
 QUERY: 7798 AAGCTCCAGCCAGCATCCGAGAGAAAGCAGGTCAGTGGTTTGGCACCACCACGCCATC 7857
 SBJCT: 7724 AAGCTCCATGCCAGCATCCGAGAGAAAGCAGGCCACTGGTTTGTACCACCACACCCATC 7783
 65
 QUERY: 7858 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC 7917
 SBJCT: 7784 ATCGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACAGGAGTGTCTAGC 7843
 70
 QUERY: 7918 ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACCTGGAC 7977
 SBJCT: 7844 ATCGCCAGTGAGGACAGCCGCAAGGTAGCATCCGTGTTGAACAATGCCTACTACTTAGAC 7903
 75
 QUERY: 7978 AAGATGCACTACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCC 8037
 SBJCT: 7904 AAGATGCACTACAGCATCGAGGGCAAGGACACACACTACTTTGTGAAGATCGGCGCCGCG 7963
 80
 QUERY: 8038 GATGGCGACCTGGTCACACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG 8097
 SBJCT: 7964 GATGGTGACCTGGTCACGCTAGGAACCACTTGGGCGCAAGGTGCTGGAGAGTGGGGTG 8023
 85
 QUERY: 8098 AACGTGACCGTGTCCAGCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAAC 8157
 SBJCT: 8024 AACGTGACGGTGTACAGCCACGCTGCTGGTGAATGGCAGGACTCGAAGGTTACCAAC 8083

QUERY: 8158 ATTGAGTTCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCGACACC 8217
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 8084 ATTGAGTTCAGTACTCCACGCTGCTGCTCAGTATCCGCTACGGCCTCACCCCGACACG 8143
 QUERY: 8218 CTGGACGAAGAGAAGGCCCGCTCCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCC 8277
 ||||||||||| |||||||||||||||||||| ||| ||||||||| ||||||||| ||||
 SBJCT: 8144 CTGGACGAAGAAAAGGCCCGCTCCTGGACCAAGCGGGACAGAGAGCCCTGGGTACTGCC 8203
 QUERY: 8278 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCGCCTGTGGACTGAG 8337
 ||||||||||| |||||||||||||||||||| ||| ||||||||| ||||||||| ||||
 SBJCT: 8204 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGCAGCCGCCTGTGGACGGAG 8263
 QUERY: 8338 GGCGAGAAGCAGCAGCTTCTGAGCACCGGGCGCGTGAAGGGTACGAGGGATATTACGTG 8397
 ||||||||||| |||||||||||||||||||| ||| ||||||||| ||||||||| ||||
 SBJCT: 8264 GGCGAGAAGCAGCAACTCCTGAGCACGGGACGGGTACAAGTTATGAGGGCTATTACGTA 8323
 QUERY: 8398 CTTCCCGTGGAGCAATACCCAGAGCTTGCGAGACAGTAGCAGCAACATCCAGTTTTTAAGA 8457
 ||||||||||| || ||||| |||||||||||||||||||| ||||||||||| ||||
 SBJCT: 8324 CTTCCGGTGAACAGTACCCGGAGCTGGCAGACAGTAGCAGCAACATCCAGTCTTAAAG 8383
 QUERY: 8458 CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCTTGTCTGAATGGCT 8517
 ||||||||||| |||||||||||||||||||| ||||||||||| ||||| ||||| ||||
 SBJCT: 8384 CAGAATGAGATGGGAAAGAGGTAACAAAATAACCTGCTGCCACCTCTTCTCTGGGTGGCT 8443
 QUERY: 8518 CAGCAGGAGTAAGTGTATCTCTCTCTCTAAGGAGATGAAGACCTAACAGGGGCAGTGG 8577
 ||||||||||| ||||| |||||||||||||||||||| ||||||||||| ||||||||| ||
 SBJCT: 8444 CAGCAGGAGCAACTGTGACCTCTCTCTCTAAGGAGACGAAGACCTAAC-GGGGCAGTGG 8502
 QUERY: 8578 GCTGGGTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8637
 || ||||||||||||| |||||||||||||||||||| ||||||||||| ||||||||| ||||
 SBJCT: 8503 GCCGGGTGCTTTAGGATCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8562
 QUERY: 8638 ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGGC 8685
 ||||| ||||| ||||||||||||| ||||||||||||| ||||||||||| ||||| ||||
 SBJCT: 8563 ACTGTCTAAGCGCAAAGTCCCTCATCCTGAAGTAGACTAGAGCCCGGC 8610
 ||||| ||||| ||||||||||||| ||||||||||||| ||||||||||| ||||| ||||
 SCORE = 1570 BITS (792), EXPECT = 0.0
 IDENTITIES = 1095/1196 (91%)
 STRAND = PLUS / PLUS
 QUERY: 270 ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG 329
 ||||||||||| |||||||||||||||||||| ||||||||||| ||||||||| |||||
 SBJCT: 103 ATCTGGAATAATGGATGTAAAGGACCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG 162
 QUERY: 330 CAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCCACACA 389
 ||||||||||| |||||||||||||||||||| ||||||||||| ||||||||| |||||
 SBJCT: 163 CAAAGAGTGTGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCACTCA 222
 QUERY: 390 GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA 449
 ||||| ||||||||||| ||||||||||||| ||||||||||||| ||||||||||| |||||
 SBJCT: 223 GAAGTCTACAGTTCAGTGAGACCTTGAAGGCTTATGACCATGACAGCAGAATGCACTA 282
 QUERY: 450 TGGAAACCGAGTCACAGACCTCATCCACCGGGAGTCAGATGAGTTTCTAGACAAGGAAC 509
 ||||||||||| |||||||||||||||||||| ||||||||||| ||||||||| |||||
 SBJCT: 283 TGGAAACCGAGTCACAGACCTGGTGCACCGGGAGTCCGATGAGTTTCTAGACAAGGGAC 342
 QUERY: 510 CAACTTCACCTTGCCGAAGTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569
 ||||||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
 SBJCT: 343 AAAGTTCACCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 402
 QUERY: 570 CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629
 SBJCT: 403 TTCCGACATGGGTATCTTCCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCAGACTC 462
 QUERY: 630 CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689
 SBJCT: 463 GGACACCGAGGGAGGGATGTCTCCAGAACATGCCATCAGACTGTGGGGCAGAGGGATAAA 522

QUERY: 690 ATCCAGGCGCAGTTCGGGCTGTCCAGTCGTGAAAACCTGGCCCTTACCCTGACTGACTC 749
 |||||
 SBJCT: 523 ATCCAGGCGCAGCTCTGGCTTGTCCAGCCGCGAGAACTCGGCCCTTACTCTGACTGACTC 582
 |||||
 QUERY: 750 TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCACCTACATCCTCGCC 809
 |||||
 SBJCT: 583 TGACAAATGAAAATAAATCGGATGACGACAATGGTCGTCCCATTCACCTACATCCTCGTC 642
 |||||
 QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAAATCCTCCACCAGTTAGCTGCCA 869
 |||||
 SBJCT: 643 TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAAATCCTCCACCAGTTAGCTGCCA 702
 |||||
 QUERY: 870 GATGCCATTGCTAGACAGCAACACCTCCCATCAAATCATGGACACCAACCTGATGAGGA 929
 |||||
 SBJCT: 703 GATGCCATTGCTAGACAGCAACACCTCCCATCAGATCATGGACACCAACCTGATGAGGA 762
 |||||
 QUERY: 930 ATTCTCCCCCAATTACATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
 |||||
 SBJCT: 763 ATTCTCCCCCAATTACATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 822
 |||||
 QUERY: 990 TGGCCCTCCGAACCACACAGCCAGTCGACTCTGAGGCCCCCTCTCCACCCCTCACAA 1049
 |||||
 SBJCT: 823 TGGCCCTCCAAACCACACAGCCAGTCAACACTGAGGCCCCCTCTGCCACCCCTCATAA 882
 |||||
 QUERY: 1050 CCACACGCTGTCCCATCACCCTCGTCCGCCAACTCCCTCAACAGGAACTCACTGACCAA 1109
 |||||
 SBJCT: 883 CCACACCTGTCCCAACCACCTCCTCGGCCAACTCCCTCAACAGGAACTCACTGACCAA 942
 |||||
 QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCCGGCCCCAGCGCCCAATGACCTGGCCACCACACCAGA 1169
 |||||
 SBJCT: 943 TCGGCGGAGTCAAATCCACGCCCCAGCTCCTGCGCCCAACGACCTGGCCACCACCCAGA 1002
 |||||
 QUERY: 1170 GTCCGTTTCACTTCAAGACCTCCTCGGGAGCACACCTTGTTCAGCAGCTCTTCCCGGGATA 1229
 |||||
 SBJCT: 1003 GTCTGTTTCACTTCCAGGATAGCTGGGTGCTGAACAGTAACGTCCCACTGGAGACTCGGCA 1062
 |||||
 QUERY: 1230 CTTCTCTTCAAGACCTCCTCGGGAGCACACCTTGTTCAGCAGCTCTTCCCGGGATA 1289
 |||||
 SBJCT: 1063 CTTCTCTTCAAAACGTCGTCTGGAAGCACACCCCTGTTTCAAGCAGCTCTTCTCCGGGATA 1122
 |||||
 QUERY: 1290 CCCTTTGACCTCAGGAACGGTTTACACGCCCCCGCCCGCTGCTGCCAGGAATACTTT 1349
 |||||
 SBJCT: 1123 CCCTTTGACCTCAGGACCGTTTATACACCACACCCCGCTGCTGCCAGGAATACATT 1182
 |||||
 QUERY: 1350 CTCCAGGAAGGCCTTTCAAGCTGAAGAAGCCCTCAAATACTGCAGCTGGAAATGTGCTGC 1409
 |||||
 SBJCT: 1183 CTCCAGGAAGGCCTTCAAGCTGAAGAAACCTCAAATACTGCAGTTGGAAATGTGCTGC 1242
 |||||
 QUERY: 1410 CCTCTCCGCCATTGCCGCGGCCCTCCTCTTGGCTATTTTGTGGCGTATTTTCATAG 1465
 |||||
 SBJCT: 1243 CCTGTCTGCCATCGCCGCGCCCTCCTCTTGGCCATTTTGTGGCATATTTTCATAG 1298
 |||||
 SCORE = 1455 BITS (734), EXPECT = 0.0
 IDENTITIES = 1000/1088 (91%), GAPS = 3/1088 (0%)
 STRAND = PLUS / PLUS
 QUERY: 1464 AGTGCCCTGGTCGTTGAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
 |||||
 SBJCT: 1420 AGTGCCCTGGTCATTGAAAACAGCAGCATAGACAGTGGCGAAGCAGAAGTTGGTCGGCG 1479
 |||||
 QUERY: 1524 GGTAAACACAAGAAGTCCACCAGGGGTGTTTTGGAGGTCAAAATTCACATCAGTCAGCC 1583
 |||||
 SBJCT: 1480 GGTGACACAGGAAGTCCACCAGGGGTGTTTTGGAGGTCCAGATTACATCAGTCAGCC 1539
 |||||
 QUERY: 1584 CCAGTTCTTAAAGTTCAACATCTCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAG 1643
 |||||
 SBJCT: 1540 TCAATTCTTAAAGTTCAACATCTCCCTCGGGAAGGATGCCCTCTTCGGTGTCTATATAAG 1599
 |||||

5
 QUERY: 1644 AAGAGGACTTCCACCATCTCATGCCAGTATGACTTCATGGAACGTCTGGACGGGAAGGA 1703
 SBJCT: 1600 GAGAGGACTACCACCGTCTCATGCCAGTATGACTTCATGGAACGCCTGGATGGAAAGGA 1659
 10
 QUERY: 1704 GAAGTGGAGTGTGGTTGAGTCTCCAGGGAACGCCGAGCATACAGACCTTGGTTTCAGAA 1763
 SBJCT: 1660 GAAATGGAGCGTGGTCGAGTCGCCCAGGGAACGCCGAGCATCCAGACTCTGGTGCAGAA 1719
 15
 QUERY: 1764 TGAAGCCGTGTTTGTGCAGTACCTGGATGTGGGCCTGTGGCATCTGGCCTTCTACAATGA 1823
 SBJCT: 1720 CGAGGCTGTGTTTGTGCAGTACTTGGATGTGGGCCTGTGGCACCTGGCCTTCTACAATGA 1779
 20
 QUERY: 1824 TGGAAAAGACAAAGAGATGGTTTCCTTCAATACTGTTGTCTTAGATTTCAGTGCAGGACTG 1883
 SBJCT: 1780 CGGCAAGGACAAGGAGATGGTCTCCTTCAACACTGTTGTCTTAGATTTCAGTGCAGGACTG 1839
 25
 QUERY: 1884 TCCACGTAACCTGCCATGGGAATGGTGAATGTGTGTCCGGGGTGTGTCACTGTTTCCCAGG 1943
 SBJCT: 1840 TCCACGGAACTGTACCGGGAACGGTGAATGCGTGTCTGGACTGTGTCACTGTTTCCCAGG 1899
 30
 QUERY: 1944 ATTCTTAGGAGCAGACTGTGCTAAAGCTGCCTGCCCTGTCTGTGCAGTGGGAATGGACA 2003
 SBJCT: 1900 ATTCTTAGGTGCAGACTGTGCTAAAGCTGCCTGCCCTGTACTGTGCAGCGGAAATGGACA 1959
 35
 QUERY: 2004 ATATTCTAAAGGGACGTGCCAGTGCTACAGCGGTGGAAGGTGCAGAGTGCACGTGCC 2063
 SBJCT: 1960 GTATTCTAAAGGAACGTGCCAGTGCTACAGCGGTGGAAGGTGCAGAGTGTGATGTGCC 2019
 40
 QUERY: 2064 CATGAATCAGTGCATCGATCCTTCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACTG 2123
 SBJCT: 2020 TATGAACCAATGTATCGATCCTTCTGCGGGGGCCATGGCTCCTGCATTGATGGGAACTG 2079
 45
 QUERY: 2124 TGTCTGCTCTGCTGGCTACAAAGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCAC 2183
 SBJCT: 2080 CGTGTGTGCTGCTGGCTACAAGGGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCTAC 2139
 50
 QUERY: 2184 CTGCTCCAGCCACGGAGTCTGTGTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGG 2243
 SBJCT: 2140 CTGCTCCAGCCATGGTGTCTGTGTGAATGGAGAGTGTCTATGCAGCCCCGGCTGGGGTGG 2199
 55
 QUERY: 2244 TCTGAACGTGTGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGCAGTGGGCATGGCACGTA 2303
 SBJCT: 2200 TCTCAACTGTGAGCTGGCGAGGGTCCAGTGCCAGACCAGTGTAGTGGGCATGGCACTTA 2259
 60
 QUERY: 2304 CCTGCCTGACACGGGCCCTCTGCAGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGT 2363
 SBJCT: 2260 CCTCCCTGACTCCGGCCTCTGCAGCTGTGATCCGAAGTGGATGGGTCCCGACTGCTCTGT 2319
 65
 QUERY: 2364 TGAAGTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2423
 SBJCT: 2320 T---GTGTGCTCAGTAGACTGTGGCACTCACGGCGTCTGCATCGGGGGAGCCTGCCGCTG 2376
 70
 QUERY: 2424 TGAAGAGGGCTGGACAGGCGCAGCGTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2483
 SBJCT: 2377 TGAAGAGGGCTGGACAGGCGCAGCTTGTGACCAGCGCGTGTGCCACCCCGCTGCATTGA 2436
 75
 QUERY: 2484 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2543
 SBJCT: 2437 GCACGGGACCTGTAAAGATGGCAAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTG 2496
 80
 QUERY: 2544 CACCATTG 2551
 SBJCT: 2497 CACCATTG 2504
 SCORE = 105 BITS (53), EXPECT = 5E-19
 IDENTITIES = 81/89 (91%), GAPS = 1/89 (1%)
 STRAND = PLUS / PLUS

SBJCT: 2947 AATGTGTCTTTTGTCAAGTACCCAAAATATGGCTACACCATCACTCGCCAGGACGGCAGC 3006
 QUERY: 3058 TTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAGCGAGCCCCGTTTC 3117
 SBJCT: 3007 TTTGACCTGATTGCCAATGGGGGCTCTGCCTTGACTCTTCACTTTGAGCGAGCCCCCTTTC 3066
 QUERY: 3118 ATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCCATGGACACCTTG 3177
 SBJCT: 3067 ATGAGCCGGGAGCGCACAGTATGGCCGCCGTGGAACAGCTTCTATGCCATGGACACCTTG 3126
 QUERY: 3178 GTGATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3237
 SBJCT: 3127 GTAATGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGCTTTGTCCGGCCT 3186
 QUERY: 3238 GATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCCCCCTGGGCAGAAT 3297
 SBJCT: 3187 GATCCGATCATCATCTCCTCTCCTGTCCACCTTCTTCAGCGCTTCCCTGCGGCGAAC 3246
 QUERY: 3298 CCCATCGTGCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCTGGTTCCAATGTG 3357
 SBJCT: 3247 CCCATTGTGCCTGAGACCCAGGTTCTTCATGAGGAGATCGAGCTCCCTGGCACCAACGTG 3306
 QUERY: 3358 AAACCTCGCTATCTGAGCTCTAGAAGTGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3417
 SBJCT: 3307 AAGCTCCGTTACCTCAGCTCCAGAACAGCAGGGTACAAGTCACTGCTGAAGATCACCATG 3366
 QUERY: 3418 ACCCAGTCCACAGTGCCCTGAACCTCATTAGGGTTACCTGATGGTGGCTGTGAGGGG 3477
 SBJCT: 3367 ACCCAGTCCACGGTGCCCTTGAACCTCATCCGGGTTCACCTTGATGGTGGCTGGAGGGG 3426
 QUERY: 3478 CATCTCTTCCAGAAGTCATTCAGGCTTCTCCCAACCTGGCCTCCACCTTCATCTGGGAC 3537
 SBJCT: 3427 CATCTCTTCCAGAAGTCGTTCCAGGCTTCTCCCAACCTGGCCTACACATTCATCTGGGAC 3486
 QUERY: 3538 AAGACAGATGCGTATGGCCAAAGGGTGTATGGACTCTCAGATGCTGTTGTGTCTGTGCGG 3597
 SBJCT: 3487 AAGACAGACGCTTATGGCCAAAGGGTTTATGGCTATCGGATGCTGTTGTGTCTGTGGA 3546
 QUERY: 3598 TTTGAATATGAGACCTGTCCAGTCTAATTCTCTGGGAGAAAAGGACAGCCCTCCTTCAG 3657
 SBJCT: 3547 TTTGAATATGAGACCTGCCCCAGTCTCATCCTGTGGGAAAAAGGACAGCCCTACTTCAA 3606
 QUERY: 3658 GGATTCGAGCTGGACCCCTCCAACCTCGGTGGCTGGTCCCTAGACAAACACCACATCCTC 3717
 SBJCT: 3607 GGATTCGAGCTGGACCCCTCCAACCTTGGTGGCTGGTCCCTGGATAAGCACACACCTC 3666
 QUERY: 3718 AATGTTAAAAGTGAATCCTACACAAAGGCACTGGGGAAAACAGTTTCTGACCCAGCAG 3777
 SBJCT: 3667 AATGTGAAAAGCGGAATACTACTCAAAGGCACAGGGGAGAACCAGTTCTGACCCAGCAG 3726
 QUERY: 3778 CCTGCCATCATCACCAGCATCATGGGCAATGGTGCCTGCGCCGAGCATTCTCTGTCCCAGC 3837
 SBJCT: 3727 CCGCCATCATCACCAGCATCATGGGTAACGGTGCCTGCGCAGAACATCTCTGTCCCAGC 3786
 QUERY: 3838 TGCAACGGCCTTGCTGAAGGCAACAAGCTGTGGCCCCAGTGGCTCTGGCTGTTGGAATC 3897
 SBJCT: 3787 TGCAATGGCCTTGCTGAAGGCAACAAGCTGTTGGCCCCGTGGCCCTGGCTGTGGGGATC 3846
 QUERY: 3898 GATGGGAGCCTCTATGTGGGTGACTTCAATTACATCCGACGCATCTTCCCTCTCGAAAT 3957
 SBJCT: 3847 GATGGGAGCCTCTTGTGCGTGACTTCAATTATATCCGCGCATCTTCCCTTCTCGAAAC 3906
 QUERY: 3958 GTGACCAGCATCTTGAGTTACGAAATAAAGAGTTTAAACATAGCAACAACCCAGCACAC 4017
 SBJCT: 3907 GTGACCAGTATCTTGAGTTACGAAATAAAGAGTTTAAACATAGCAACAGCCAGGACAC 3966
 QUERY: 4018 AAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCTACGTGTCCGACCAACAGC 4077

SBJCT: 3967 AAGTACTACTTGGCTGTGGACCCTGTGACTGGCTCGCTCTATGTCTCTGACACCAACAGT 4026
 QUERY: 4078 AGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAAACAAAGACCTGGCTGGGAATTCGGAA 4137
 SBJCT: 4027 CGCCGGATCTACCGAGTCAAGTCTCTAAGCGGAGCCAAAGACCTGGCTGGGAATTCGGAA 4086
 QUERY: 4138 GTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCCTTTGATGAAGCCCGCTGCGGGGATGGA 4197
 SBJCT: 4087 GTTGTGGCCGGGACTGGCGAACAATGTCTACCCCTTTGATGAAGCCCGCTGTGGGGATGGC 4146
 QUERY: 4198 GGGGAAGGCCATAGATGCAACCTGATGAGCCCGAGAGGTATTGCAGTAGACAAGAATGGG 4257
 SBJCT: 4147 GGGGAAGGTGTGGATGCCACCCTGATGAGCCCTAGAGGTATTGCAGTAGACAAGAACGGG 4206
 QUERY: 4258 CTCATGTACTTTGTGCGATGCCACCATGATCCGGAAGGTTGACCAGAATGGAATCATCTCC 4317
 SBJCT: 4207 CTTATGTATTTTGTGATGCCACCATGATCCGGAAGGTCGACCAAATGGAATCATCTCC 4266
 QUERY: 4318 ACCCTGCTGGGCTCCAATGACCTCACTGCGCTCCGGCCGCTGAGCTGTGATTCCAGCATG 4377
 SBJCT: 4267 ACCCTGCTGGGCTCCAATGACCTCACTGCTCCGACCACTGAGCTGTGACTCTAGCATG 4326
 QUERY: 4378 GATGTAGCCCAGGTTCTGCTGGAGTGGCCAACAGACCTTGCTGTCAATCCCATGGATAAC 4437
 SBJCT: 4327 GACGTGGCCAGGTCCGTCTAGAATGGCCGACAGACCTTGCGGTCAACCCCATGGACAAT 4386
 QUERY: 4438 TCCTTGATGTTCTAGAGAACAATGTCATCCTTCGAATCACCGAGAACCACCAAGTCAGC 4497
 SBJCT: 4387 TCCTTGATGTTCTAGAGAACAACGTATCCTGCGGATCACCGAGAATCACCGAGTCAGC 4446
 QUERY: 4498 ATCATTGCGGGACGCCCCATGCACTGCCAAGTTCCTGGCATTGACTACTCACTCAGCAA 4557
 SBJCT: 4447 ATCATGCGGGACGCCCCATGCACTGCCAGGTTCCCGGCATCGACTACTCGCTCAGCAAG 4506
 QUERY: 4558 CTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTGCCATTTCTCACACTGGGGTC 4617
 SBJCT: 4507 CTCGCCATCCACTCTGCTCTGGAGTCAGCCAGCGCCATCGCCATTTCTCACACCGGGTG 4566
 QUERY: 4618 CTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTCTACGCCAGGTAACAACCAAC 4677
 SBJCT: 4567 CTCTACATCACCGAGACGAGCAGAGAAGAAGATCAACCGCTACGCCAGGTACCAACCAAC 4626
 QUERY: 4678 GGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCGACTGCAAAAACGATGTCAAT 4737
 SBJCT: 4627 GGAGAGATCTGCCTCTTAGCCGGGGCAGCCTCAGACTGTGACTGCAAAAATGACGTCAAC 4686
 QUERY: 4738 TGCAACTGCTATTCAAGAGATGATGCCTACGCGACTGATGCCATCTGAATTCCCATCA 4797
 SBJCT: 4687 TGCATCTGCTATTTCGGGAGATGACGCATACGCCACGGATGCCATCTGAATCCCGTCC 4746
 QUERY: 4798 TCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAGACCTTGGAATATTTCGGATC 4857
 SBJCT: 4747 TCCTTAGCTGTGGCTCCGGATGGCACCATCTACATCGCAGACCTCGGAATATCCGGATC 4806
 QUERY: 4858 AGGGCGGTCAGCAAGAACAAGCCTGTTCTTAATGCCTTCAACCAGTATGAGGCTGCATCC 4917
 SBJCT: 4807 AGGGCGGTCAGCAAAAACAACCTGTTCTTAACGCGTTCAACCAGTATGAGGCTGCGTCT 4866
 QUERY: 4918 CCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCATCCACCAATACACTGTGAGC 4977
 SBJCT: 4867 CCGGAGAACAGGAACTGTACGTGTTCAACGCGATGGTATCCATCAGTACACCGTGAGC 4926
 QUERY: 4978 CTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTACTGACAATGATGTCACTGAA 5037
 SBJCT: 4927 CTGGTGACCGGGAGTACTTATACAATTTACCTACAGCGCTGACAATGATGTCAACGAG 4986
 QUERY: 5038 TTGATTGACAATAATGGGAATTCCTGAAGATCCGTCGGGACAGCAGTGGCATGCCCCGT 5097

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QUERY: 6058 AGCGTGGCCCGGCACAGCATGTCCACACACACCTCCATCGGCTACATCCGTAATTATTAC 6117
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SBJCT: 6007 AGTTGTCGCCCGGCACAGCATGTCCACGCACACCTCCATTGGCTACATCCGGAACATTTC 6066

QUERY: 6118 AACCCGCCTGAAAGCAATGCTTCGGTCATCTTTGACTACAGTGATGACGGCCGCATCCTG 6177
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SBJCT: 6067 AACCCACCGGAAAGCAACGCCTCGGTATCTTTGACTACAGTGATGACGGCCGCATCCTG 6126

QUERY: 6178 AAGACCTCCTTTTTGGGCACCGGACGCCAGGTGTTCTACAAGTATGGGAACTCTCCAAG 6237
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SBJCT: 6127 AAGACGTCTTTCTGGGCACCGGGCGCAGGTGTTCTATAAGTACGAAAACTGTCCAAG 6186

QUERY: 6238 TTATCAGAGATTGCTCTACGACAGTACCGCCGTACCTTCGGGTATGACGAGACCACTGGT 6297
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SBJCT: 6187 TTATCGGAGATCGTCTACGACAGCACTGCCGTACCTTCGGCTATGACGAGACCACTGGC 6246

QUERY: 6298 GTCTTGAAGATGGTCAACCTCCAAAGTGGGGGCTTCTCTGCACCATCAGGTACCGAAG 6357
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SBJCT: 6247 GTCCTGAAGATGGTGAATCTCCAAAGCGGGGGCTTCTCTGTACCATCAGGTACCGAAAAG 6306

QUERY: 6358 ATTGGCCCCCTGGTGGACAAGCAGATCTACAGTTCTCCGAGGAAGGCATGGTCAATGCC 6417
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SBJCT: 6307 GTCGGGCCCCCTCGTGGACAAGCAGATTTACAGTTCTCTGAGGAAGGCATGATCAACGCC 6366

QUERY: 6418 AGGTTTGACTACACCTATCATGACAACAGCTTCCGCATCGCAAGCATCAAGCCCCTCATA 6477
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6367 AGGTTTCGATTACACCTACCACGACAACAGCTTCCGCATCGCCAGCATCAAGCCCCTCATC 6426

QUERY: 6478 AGTGAGACTCCCTCCCGTTGACCTCTACCGCTATGATGAGATTCTGGCAAGGTGGAA 6537
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SBJCT: 6427 AGTGAGACTCCCTTCCCGTTGACCTCTACCGCTACGATGAGATTCTGGCAAGGTGGAA 6486

QUERY: 6538 CACTTTGGTAAGTTTGGAGTCATCTATTATGACATCAACCAGATCATCACCACTGCCGTG 6597
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SBJCT: 6487 CACTTCGGCAAGTTTCGGGGTCATCTACTACGACATCAACCAGATCATCACCACTGCCGTC 6546

QUERY: 6598 ATGACCCTCAGCAAACACTTCGACACCCATGGGCGGATCAAGGAGGTCCAGTATGAGATG 6657
|| || || || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6547 ATGACACTCAGCAAGCACTTTGACACCCATGGGCGCATCAAGGAAGTGCAGTATGAGATG 6606

QUERY: 6658 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGCATGGGCAGGGTGATCAAG 6717
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6607 TTCCGGTCCCTCATGTACTGGATGACGGTGCAATATGACAGTATGGGCAGGGTGATCAAG 6666

QUERY: 6718 AGGGAGCTAAAACTGGGGCCCTATGCCAATACCAGAAGTACACCTATGACTACGATGGG 6777
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SBJCT: 6667 AGGGAAC TGAACTGGGGCCCTATGCCAACACCACAAAGTACACCTATGACTACGACGGG 6726

QUERY: 6778 GACGGGCAGCTCCAGAGCGTGGCCGTCAATGACCGCCCGACCTGGCGCTACAGCTATGAC 6837
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6727 GACGGCCAGCTCCAGAGTGTGGCCGTCAATGACCGGCCTACCTGGCGTTATAGCTATGAC 6786

QUERY: 6838 CTTAATGGGAATCTCCACTTACTGAACCCAGGCAACAGTGTGCGCCTCATGCCCTTGCGC 6897
|| || || || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6787 CTC AATGGGAACCTGCACCTGCTAAACCCAGGAAACAGTGCTCGCCTCATGCCGTTACGC 6846

QUERY: 6898 TATGACCTCCGGGATCGGATAAACCAGACTCGGGGATGTGCAGTACAAAATTGACGACGAT 6957
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6847 TATGACCTCCGTGACCGGATAAACCAGGCTAGGGGACGTGCAGTACAAAATCGATGATGAT 6906

QUERY: 6958 GGCTATCTGTGCCAGAGAGGGTCTGACATCTTGAATACAATTCGAAGGGCCTCTAACA 7017
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6907 GGCTATTTATGCCAGAGAGGATCTGACATCTTTGAATACAACCTCAAGGGCCTCTAACG 6966

QUERY: 7018 AGAGCCTACAACAAGGCCAGCGGGTGGAGTGTCAGTACCGCTATGATGGCGTAGGACGG 7077
|||| | || || || || || || || || || || || || || || || || || || || || || || || || || || || ||
SBJCT: 6967 AGAGCGTACAACAAGGCCAGCGGGTGGAGTGTGAGTACCGCTATGATGGCGTGAGCCGC 7026

QUERY: 7078 CCGGCTTCTCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTACTCTGACCTCCAC 7137
 |||||
 SBJCT: 7027 CGGGCTTCTCTACAAGACCAACCTGGGCCACCACCTGCAGTACTTCTATTCCGACCTCCAC 7086
 QUERY: 7138 AACCCGACGCGCATCACCCATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTAC 7197
 |||||
 SBJCT: 7087 CACCCACACGTATCACCCATGTTTACAACCACTCCAACCTCTGAGATCACTCACTCTAC 7146
 QUERY: 7198 TACGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTT 7257
 |||||
 SBJCT: 7147 TATGACCTCCAGGGCCACCTCTTTGCCATGGAGAGCAGTAGTGGGGAAGAGTACTATGTT 7206
 QUERY: 7258 GCCTCTGATAACACAGGGACTCCTCTGGCTGTGTTTCTGAGTCAACGGCCTCATGATCAAA 7317
 |||||
 SBJCT: 7207 GCCTCAGATAACACCGGGACTCCTCTGGCTGTGTTTCTGATCAATGGCCTCATGATCAAG 7266
 QUERY: 7318 CAGCTGCAGTACACGGCCTATGGGGAGATTTATTTATGACTCCAACCCCGACTTCCAGATG 7377
 |||||
 SBJCT: 7267 CAACTCCAATACACAGCCTATGGGGAGATTTACTATGACTCCAATCCAGACTTTCAGATG 7326
 QUERY: 7378 GTCATTGGCTTCCATGGGGGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAG 7437
 |||||
 SBJCT: 7327 GTCATCGGCTTCCACGGAGGCCTCTACGACCCCTCACCAGCTCGTTCACTTTACGCAG 7386
 QUERY: 7438 CGTGATTATGATGTGCTGGCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAAC 7497
 |||||
 SBJCT: 7387 CGTGATTATGACGTGCTGGCAGGACGCTGGACGCTCCCCGACTACACCATGTGGAGGAAT 7446
 QUERY: 7498 GTGGGCAAGGAGCCGGCCCCCTTTAACTGTATATGTTTCAAGAGCAACAATCCTCTCAGC 7557
 |||||
 SBJCT: 7447 GTGGGCAAGGAGCCAGCCCCCTTCAACTGTACATGTTTCAAGAAACAACAATCCACTCAGT 7506
 QUERY: 7558 AGTGAGCTAGATTTGAAGAACTACGTGACAGATGTGAAAAGCTGGCTTGTGATGTTTGA 7617
 |||||
 SBJCT: 7507 AATGAGCTGGATTTAAAGAACTACGTGACAGACGTGAAGAGCTGGCTCGTGATGTTTGA 7566
 QUERY: 7618 TTTCAGCTTAGCAACATCATTCCTGGCTTCCCGAGAGCCAAAATGTATTTCTGTCCTCCT 7677
 |||||
 SBJCT: 7567 TTTCAGCTCAGCAACATCATTCCTGGATTCCCAAGAGCCAAAATGTATTTGTGTCCTCCC 7626
 QUERY: 7678 CCCTATGAATTGTCTAGAGAGTCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAA 7737
 |||||
 SBJCT: 7627 CCCTATGAACTGTCTAGAGAGCCAAGCAAGTGAGAATGGACAGCTCATTACAGGTGTCCAG 7686
 QUERY: 7738 CAGACAACAGAGAGACATAACCAGGCCTTCTATGGCTCTGGAAGGACAGGTCACTACTAAA 7797
 |||||
 SBJCT: 7687 CAGACAACAGAGAGGACATAACCAGGCCTTCTATGGCTCTAGAAGGACAGGTCACTCTAAA 7746
 QUERY: 7798 AAGTCCACGCCAGCATCCGAGAGAAAGCAGGTCACTGGTTTGCCACCACCACGCCCATC 7857
 |||||
 SBJCT: 7747 AAGTCCATGCAGGCATCCGAGAGAAAGCAGGCCACTGGTTTGCTACGACCACGCCCATC 7806
 QUERY: 7858 ATTGGCAAAGGCATCATGTTTGCCATCAAAGAAGGGCGGGTGACCACGGGCGTGTCCAGC 7917
 |||||
 SBJCT: 7807 ATCGGCAAAGGCATCATGTTTCGCCATCAAAGAAGGGCGGGTGACCACAGGCGTGTCTAGC 7866
 QUERY: 7918 ATCGCCAGCGAAGATAGCCGCAAGGTGGCATCTGTGCTGAACAACGCCTACTACTGGAC 7977
 |||||
 SBJCT: 7867 ATCGCCAGTGAGGACAGCCGCAAGGTAGCATCCGTGTTGAACAACGCCTACTACTGGAC 7926
 QUERY: 7978 AAGATGCATACAGCATCGAGGGCAAGGACACCCACTACTTTGTGAAGATTGGCTCAGCC 8037
 |||||
 SBJCT: 7927 AAGATGCATACAGCATCGAGGGCAAGGACACACACTACTTTCGTGAAGATCGGTGCAGCG 7986
 QUERY: 8038 GATGGCGACCTGGTCACTAGGCACCACCATCGGCCGCAAGGTGCTAGAGAGCGGGGTG 8097
 |||||
 SBJCT: 7987 GACGGTGACCTGGTTACGCTGGGGACCACCATTTGGGCGCAAGGTGCTGGAGAGCGGGGTG 8046

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QUERY: 8098 AACGTGACCGTGTCCACCGCCACGCTGCTGGTCAACGGCAGGACTCGAAGGTTACGAAC 8157
      |||||
SBJCT: 8047 AACGTGACCGTGTCTCACAGCCCACGCTGCTGGTGAACGGCAGGACTCGAAGGTTACCAAC 8106

QUERY: 8158 ATTGAGTTCCAGTACTCCACGCTGCTGCTCAGCATCCGCTATGGCCTCACCCCCGACACC 8217
      |||||
SBJCT: 8107 ATTGAATTCCAGTACTCCACGCTGCTGCTCAGCATACGCTACGGCCTCACCCCCGACACA 8166

QUERY: 8218 CTGGACGAAGAGAAGGCCCGCTCCTGGACCAGGCGAGACAGAGGGCCCTGGGCACGGCC 8277
      |||||
SBJCT: 8167 CTGGATGAAGAGAAGGCCCGCTCCTGGACCAAGCGCGACAGAGGGCCCTGGGTACTGCC 8226

QUERY: 8278 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCCTGTGGACTGAG 8337
      |||||
SBJCT: 8227 TGGGCCAAGGAGCAGCAGAAAGCCAGGGACGGGAGAGAGGGGAGCCCTGTGGACGGAG 8286

QUERY: 8338 GGCAGAGAAGCAGCAGCTTCTGAGCACCGGGCGCTGCAAGGGTACGAGGGATATTACGTG 8397
      |||||
SBJCT: 8287 GGCAGAGAAGCAGCAACTCTTGAGCACGGGACGGGTGCAAGGTTATGAGGGCTATTACGTG 8346

QUERY: 8398 CTTCCCGTGGAGCAATACCCAGAGCTTGCGACAGTAGCAGCAACATCCAGTTTAAAGA 8457
      |||||
SBJCT: 8347 CTTCCGTTGAACAGTACCCAGAGCTGGCAGACAGTAGCAGCAACATCCAGTTCCTAAGA 8406

QUERY: 8458 CAGAATGAGATGGGAAAGAGGTAACAAAATAATCTGCTGCCATTCTTGTCTGAATGGCT 8517
      |||||
SBJCT: 8407 CAGAATGAGATGGGAAAGAGGTAACAAAATAACCTGCTGCCACCTCTTCTCTGGGTGGCT 8466

QUERY: 8518 CAGCAGGAGTAAGTGTATCTCTCTCTCTTAAGGAGATGAAGACCTAACAGGGGCACCTGCG 8577
      |||||
SBJCT: 8467 CAGCAGGAGCAACTGTGACCTCTCTCTCTTAAGGAGACGAAGACCTAACAGGGGCACCTGAG 8526

QUERY: 8578 GCTGGGCTGCTTTAGGAGACCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8637
      |||||
SBJCT: 8527 GCCGGGCTGCTTTAGGACCCCAAGTGGCAAGAAAGCTCACATTTTTTGAGTTCAAATGCT 8586

QUERY: 8638 ACTGTCCAAGCGAGAAGTCCCTCATCCTGAAGTAGACTAAAGCCCGCTGAAAATCCGA 8697
      |||||
SBJCT: 8587 ACTGTCCAAGCGCAAAGTCCCTCATCCTGAAGTAGACTAGAGCTCGGCCACAAATCTGA 8646

QUERY: 8698 GGAAAACAAAAC 8709
      |||||
SBJCT: 8647 GGAAAACAAAAC 8658

SCORE = 1459 BITS (736), EXPECT = 0.0
IDENTITIES = 1081/1196 (90%)
STRAND = PLUS / PLUS

QUERY: 270 ATCTGGAATAATGGATGTAAAGGACCGGCGACACCGCTCTTTGACCAGAGGACGCTGTGG 329
      |||||
SBJCT: 123 ATCTGCAATAATGGATGTGAAGGATCGGCGACATCGCTCTTTGACCAGGGGACGGTGTGG 182

QUERY: 330 CAAAGAGTGTGCTACACAAGCTCCTCTCTGGACAGTGAGGACTGCCGGGTGCCACACA 389
      |||||
SBJCT: 183 CAAGGAGTGTGCTACACCAGCTCCTCTCTGGACAGTGAGGACTGCCGTGTGCCACGCA 242

QUERY: 390 GAAATCCTACAGCTCCAGTGAGACTCTGAAGGCCTATGACCATGACAGCAGGATGCACTA 449
      |||||
SBJCT: 243 GAAGTCTACAGTTCCAGTGAGACCTGAAGGCTTATGACCATGACAGCAGAAATGCACTA 302

QUERY: 450 TGGAACCGAGTCACAGACCTCATCCACCGGAGTCAGATGAGTTTCTAGACAAGGAAC 509
      |||||
SBJCT: 303 TGGAACCGAGTCACAGACCTGGTGCACCGGAGTCCGATGAGTTTCTAGACAAGGGGC 362

QUERY: 510 CAACTTCACCTTGCCGAACCTGGGCATCTGTGAGCCCTCCCCACACCGAAGCGGCTACTG 569
      |||||
SBJCT: 363 TAAATTCACCTGGCAGAATTGGGAATCTGCGAGCCCTCCCCACACCGAAGTGGTTACTG 422

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QUERY: 570 CTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTTAGCACAGGGTCTGACGCCGACTC 629
 SBJCT: 423 TTCCGACATGGGGATCCTTCACCAGGGCTACTCCCTGAGCACTGGGTCTGATGCGGACTC 482
 5
 QUERY: 630 CGACACCGAGGGAGGGATGTCTCCAGAACACGCCATCAGACTGTGGGGCAGAGGGATAAA 689
 SBJCT: 483 GGACACCGAGGGAGGGATGTCTCCAGAACATGCCATCAGACTGTGGGGACGAGGGATAAA 542
 10
 QUERY: 690 ATCCAGGCGCAGTTCCGGCCTGTCCAGTCGTGAAACTCGGCCCTTACCCTGACTGACTC 749
 SBJCT: 543 ATCGAGGCGCAGCTCTGGCTTGTCAGCCGCGAGAACTCAGCCCTTACTCTGACTGATTC 602
 15
 QUERY: 750 TGACAACGAAAACAAATCAGATGATGAGAACGGTCGTCCCATTCCACCTACATCCTCGCC 809
 SBJCT: 603 TGACAATGAAATAAATCGGATGACGACAATGGTCGACCCATTCCACCTACATCCTCGTC 662
 20
 QUERY: 810 TAGTCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAACTCCTCCACCAGTTAGCTGCCA 869
 SBJCT: 663 TAGCCTCCTCCCATCTGCTCAGCTGCCTAGCTCCCATAACTCCTCCACCAGTTAGCTGCCA 722
 25
 QUERY: 870 GATGCCATTGTCTAGACAGCAACCTCCCATCAAATCATGGACACCAACCTGATGAGGA 929
 SBJCT: 723 GATGCCATTGTCTAGACAGCAACCTCCCATCAGATCATGGACACCAACCCGATGAGGA 782
 30
 QUERY: 930 ATTCTCCCCAATTATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGCAG 989
 SBJCT: 783 ATTCTCCCCAATTATACCTGCTCAGAGCATGCTCAGGGCCCCAGCAAGCCTCCAGTAG 842
 35
 QUERY: 990 TGGCCCTCCGAACCACCACAGCCAGTCGACTCTGAGGCCCCCTCTCCACCCCCCTCACA 1049
 SBJCT: 843 TGGCCCTCCGAACCACCACAGCCAGTCAACGCTGAGGCCCCCTCTGCCACCTCCTCATA 902
 40
 QUERY: 1050 CCACACGCTGTCCCATCACCCTCGTCCGCAACTCCCTCAACAGGAACCTACTGACCAA 1109
 SBJCT: 903 CCACACCTGTCCACCACCACTCCTCTGCCAACTCCCTCAACAGAACTCACTGACCAA 962
 45
 QUERY: 1110 TCGGCGGAGTCAGATCCACGCCCGGCCAGCGCCCAATGACCTGGCCACCACACGAGA 1169
 SBJCT: 963 TCGGCGGAGTCAAATCCACGCCCGGCTCCTGCACCAATGACCTGGCCACCACGCGGA 1022
 50
 QUERY: 1170 GTCCGTTTCAAGACCTCCTCGGGAGCACACCTTGTTCAGCAGCTCTTCCCCGGGATA 1289
 SBJCT: 1023 GTCCGTTTCAAGACCTCCTCGGGAAGCACACCTTGTTCAGCAGCTCTTCTCCAGGATA 1142
 55
 QUERY: 1290 CCCTTTGACCTCAGGAACGTTTACACGCCCGCCCGCCCTGTGCCCAGGAATACTTT 1349
 SBJCT: 1143 CCCCTTGACCTCAGGACCGTTTATACACCACCACCCCGCTGTGCCACGGAATACATT 1202
 60
 QUERY: 1350 CTCCAGGAAGGCTTTCAAGCTGAAGAAGCCCTCCAAATACTGCAGCTGGAAATGTGCTGC 1409
 SBJCT: 1203 CTCTAGGAAGGCCTTCAAGCTGAAGAAACCCTCCAAATACTGCAGTTGGAAATGCGCCG 1262
 65
 QUERY: 1410 CCTCTCCGCATTGCCGCGGCCCTCCTCTTGGCTATTTTGTGCGTATTTTCATAG 1465
 SBJCT: 1263 CCTGTCTGCCATTGCCGCTGCCCTCCTCTTGGCTATTTTGTGCGTATTTTCATAG 1318
 SCORE = 1427 BITS (720), EXPECT = 0.0
 IDENTITIES = 996/1088 (91%)
 STRAND = PLUS / PLUS
 QUERY: 1464 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGTGGTGAAGCAGAAGTTGGTCGGCG 1523
 SBJCT: 1440 AGTGCCCTGGTCGTTGAAAAACAGCAGCATAGACAGCGGCGAGGCAGAAGTCGGTCGACG 1499

[illegible]

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Variable	Mean	SD	Min	Max
Age	34.5	10.2	18	65
Gender	Male	Female		
Marital Status	Married	Single		
Education	High School	College		
Occupation	Manager	Worker		
Income	\$20,000	\$30,000		
Health Status	Good	Fair		
Exercise Frequency	Weekly	Monthly		
Stress Level	Low	High		
Sleep Quality	Good	Poor		
Dietary Habits	Healthy	Unhealthy		
Alcohol Consumption	None	Occasional		
Tobacco Use	Non-smoker	Smoker		
Family Size	2	3		
Work Hours	40	50		
Commuting Time	30	45		
Home Ownership	Owner	Renter		
Neighborhood Safety	Safe	Unsafe		
Access to Healthcare	Yes	No		
Health Insurance	Private	Public		
Medical History	None	Chronic		
Genetic Predisposition	Low	High		
Environmental Exposure	Low	High		
Social Support	Strong	Weak		
Life Satisfaction	High	Low		
Overall Health Score	75	15	50	100

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SBJCT: 3866 GTATCTTCCCATCCAGGAATGTGACTAGCATATTGGAGCTGAGAAATAAAGAGTTTAAAC 3925
 QUERY: 3998 ATAGCAACAACCCAGCACACAAGTACTACTTGGCAGTGGACCCCGTGTCCGGCTCGCTCT 4057
 SBJCT: 3926 ATAGCAACAATCCTGCTCACAATACTATCTGGCCGTGGACCCCGTTTCGGGCTCCCTGT 3985
 QUERY: 4058 ACGTGTCCGACACCAACAGCAGGAGAATCTACCGCGTCAAGTCTCTGAGTGGAAACCAAAG 4117
 SBJCT: 3986 ACGTATCAGACACCAACAGCCGACGGATATACAAAGTCAAATCTCTTACTGGCACGAAAG 4045
 QUERY: 4118 ACCTGGCTGGGAATTTCGGAAGTTGTGGCAGGGACGGGAGAGCAGTGTCTACCCCTTTGATG 4177
 SBJCT: 4046 ACCTGGCTGGTAATTCTGAAGTGGTAGCGGGGACTGGAGAGCAATGCCTGCCCTTTGATG 4105
 QUERY: 4178 AAGCCCGCTGCGGGGATGGAGGGAAGGCCATAGATGCAACCCTGATGAGCCCGAGAGGTA 4237
 SBJCT: 4106 AAGCCAGATGTGGAGATGGAGGGAAGCAGTGGACGCAACCCTAATGAGTCTCTCGAGGAA 4165
 QUERY: 4238 TTGCAGTAGACAAGAATGGGCTCATGTACTTTGTTCGATGCCACCATGATCCGGAAGGTTG 4297
 SBJCT: 4166 TTGCAGTGGATAAGTATGGACTCATGTATTTTGTGATGCCACTATGATTCGAAAAGTGG 4225
 QUERY: 4298 ACCAGAATGGAATCATCTCCACCCTGCTGGGCTCCAATGACCTCACTGCCGTCCGGCCGC 4357
 SBJCT: 4226 ATCAGAATGGAATTATATCAACTCTGCTGGGCTCCAATGACCTAACTGCCGTCCGACCTC 4285
 QUERY: 4358 TGAGCTGTGATTCCAGCATGGATGTAGCCAGGTTCTGCTGGAGTGGCCAACAGACCTTG 4417
 SBJCT: 4286 TAAGCTGTGATTCCAGCATGGATGTAGCCAGGTACGGCTGGAGTGGCCTACTGATCTCG 4345
 QUERY: 4418 CTGTCAATCCCATGGATAACTCCTTGATGTTCTAGAGAACAATGTCATCCTTCGAATCA 4477
 SBJCT: 4346 CTGTGATCCCATGGACAACCTCACTTTATGTCTAGAGAACAATGTTATTTTACGATCA 4405
 QUERY: 4478 CCGAGAACCACCAAGTCAGCATCATTCGCGGACGCCCATGCACTGCCAAGTTCCTGGCA 4537
 SBJCT: 4406 CAGAAAACCATCAAGTTAGCATTATTGCTGGACGCCCATGCACTGCCAGGTTCTCTGGTA 4465
 QUERY: 4538 TTGACTACTCACTCAGCAAACTAGCCATTCACTCTGCCCTGGAGTCAGCCAGTGCCATTG 4597
 SBJCT: 4466 TAGACTACTCTCTTAGCAAACTGGCTATTCACTCCGCACTTGAATCAGCCAGTGCCATTG 4525
 QUERY: 4598 CCATTTCTCACTGCGGCTCTCTACATCACTGAGACAGATGAGAAGAAGATTAACCGTC 4657
 SBJCT: 4526 CCATCTCACACACAGGAGTCTTTACATCAGTGAGACAGATGAAAAAAAAAATTAATCGGC 4585
 QUERY: 4658 TACGCCAGGTAACAACCAACGGGGAGATCTGCCTTTTAGCTGGGGCAGCCTCGGACTGCG 4717
 SBJCT: 4586 TACGCCAGGTAACCTACCAATGGAGAAATATGCCTTCTTGAGGGGCAGCTTCAGACTGTG 4645
 QUERY: 4718 ACTGCAAAAACGATGTCAATTGCAACTGCTATTTCAGGAGATGATGCCTACGCGACTGATG 4777
 SBJCT: 4646 ATTGCAAAAATGATGTCAACTGTAATTGCTATTCTGGGGATGATGGGTATGCCACTGATG 4705
 QUERY: 4778 CCATCTTGAATTCCTCATCCTTAGCTGTAGCTCCAGATGGTACCATTACATTGCAG 4837
 SBJCT: 4706 CCATCTTAAATTACCATCTTCCTTAGCTGTGGCCCCAGATGGTACCATCTACATAGCTG 4765
 QUERY: 4838 ACCTTGGAATATTCGGATCAGGGCGGTGAGCAAGAACAAGCCTGTTCTTAATGCCTTCA 4897
 SBJCT: 4766 ATCTCGGAAATATCCGCATTAGGGCTGTGAGTAAAAACAGGCCATTCTTAATTCTTTA 4825
 QUERY: 4898 ACCAGTATGAGGCTGCATCCCCGGAGAGCAGGAGTTATATGTTTTCAACGCTGATGGCA 4957
 SBJCT: 4826 ACCAATATGAAGCTGCATCTCCAGGAGAACAGGAGCTGTATGCTTCAATGCTGATGGGA 4885
 QUERY: 4958 TCCACCAATACACTGTGAGCCTGGTGACAGGGGAGTACTTGTACAATTTACATATAGTA 5017

SBJCT: 1414 AGCAGCATAGATAGTGGAGAAACAGAAGTTGGCCGCAAGGTCACCCAAGAGGTGCCCCCT 1473
 QUERY: 1546 GGGGTGTTTTGGAGGTCACAAATTCACATCAGTCAGCCCCAGTTCTTAAAGTTCAACATC 1605
 SBJCT: 1474 GGAGTGTTCTGGCGGTCTCAGATCCATATCAGCCAGCCACAGTTCCTGAAGTTCAACATA 1533
 QUERY: 1606 TCCCTCGGGAAGGACGCTCTCTTTGGTGTTTACATAAGAAGAGGACTTCCACCATCTCAT 1665
 SBJCT: 1534 TCCCTAGGGAAGGATGCTCTTTTCGGTGTATATATAAGAAGAGGACTCCACCATCACAT 1593
 QUERY: 1666 GCCCAGTATGACTTTCATGGAACGCTCTGGACGGGAAGGAGAAGTGGAGTGTGGTTGAGTCT 1725
 SBJCT: 1594 GCACAGTATGATTTTCATGGAACGCTTGGATGGGAAAGAGAAATGGAGTGTGGTGGGAATCC 1653
 QUERY: 1726 CCCAGGGAACGCCGAGCATAACAGACCTTGGTTCAGAATGAAGCCGTGTTTGTGCAGTAC 1785
 SBJCT: 1654 CCACGGGAACGGCGAAGTATTACAGACTCTGTTTTCAGAATGAGGCTGTGTTTGTTCAGTAC 1713
 QUERY: 1786 CTGGATGTGGGCTGTGGCATCTGGCCTTCTACAATGATGGAAAAGACAAAGAGATGGTT 1845
 SBJCT: 1714 TTGGATGTGGGTTTGTGGCACCTGGCGTTTTACAATGATGGCAAGGACAAAGAAGTGGTC 1773
 QUERY: 1846 TCCTTCAATACTGTTGTCTTAGATTTCAGTGCAGGACTGTCCACGTAAGTCCCATGGGAAT 1905
 SBJCT: 1774 TCCTTCAGTACAGTTATTTTGGATTTCAGTGCAGGACTGTCCACGTAATTGTTCATGGCAAT 1833
 QUERY: 1906 GGTGAATGTGTGTCCGGGTGTGTCACTGTTTCCCAGGATTCTAGGAGCAGACTGTGCT 1965
 SBJCT: 1834 GGCGAGTGTGTTCTGTTGTCTGCCACTGTTTCCCAGGATTTCATGGAGCAGATTGTGCT 1893
 QUERY: 1966 AAAGCTGCCTGCCTGTCTGTGCAGTGGGAATGGACAATATTCTAAAGGGACGTGCCAG 2025
 SBJCT: 1894 AAAGCTGCCTGCCCGGTGCTGTGCAGTGGCAATGGTCACTACTCCAAGGAACCTGCTTG 1953
 QUERY: 2026 TGCTACAGCGGCTGGAAAGGTGCAGAGTGGCAGCTGCCCATGAATCAGTGCATCGATCCT 2085
 SBJCT: 1954 TGCTACAGTGGCTGGAAAGGTCCGGAATGTGATGTACCCATCAGCCAGTGTATTGATCCC 2013
 QUERY: 2086 TCCTGCGGGGGCCACGGCTCCTGCATTGATGGGAACGTGTGTCTGCTCTGCTGGCTACAAA 2145
 SBJCT: 2014 TCGTGTGGAGGTGATGTTTCTGCATCGAAGGGAACGTGTGTCTGTTCCATTGGCTATAAA 2073
 QUERY: 2146 GGCGAGCACTGTGAGGAAGTTGATTGCTTGGATCCCACCTGCTCCAGCCACGGAGTCTGT 2205
 SBJCT: 2074 GGAGAAAACGTGTGAGGAAGTTGATTGCTTAGATCCAACATGCTCCAATCACGGGGTCTGT 2133
 QUERY: 2206 GTGAATGGAGAATGCCTGTGCAGCCCTGGCTGGGGTGGTCTGAACTGTGAGCTGGCGAGG 2265
 SBJCT: 2134 GTGAACGGAGAATGTCTCTGCAGCCAGGCTGGGGTGGAAATAAAGTGTGAGCTTCCAGA 2193
 QUERY: 2266 GTCCAGTGCACAGACAGTGCAGTGGGCATGGCACGTACCTGCCTGACACGGGCTCTGCT 2325
 SBJCT: 2194 GCCCAGTGCACAGACAGTGCAGTGGGCATGGCACATACCTGTCTGACACCGGTCTCTGT 2253
 QUERY: 2326 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCTGTTGAAGTGTGCTCAGTAGACTGT 2385
 SBJCT: 2254 AGCTGCGATCCCAACTGGATGGGTCCCGACTGCTCCGTTGAAGTGTGCTCTGTAGACTGT 2313
 QUERY: 2386 GGCACTCACGGCGTCTGCATCGGGGAGCCTGCCGCTGTGAAGAGGGCTGGACAGGCGCA 2445
 SBJCT: 2314 GGCAACCATGGGGTGTGATTGGCGGAGCGTGTGCTGTGAAGAAGGGTGGACAGGAGTG 2373
 QUERY: 2446 GCGTGTGACCAGCGGTGTGCCACCCCGCTGCATTGAGCACGGGACCTGTAAAGATGGC 2505
 SBJCT: 2374 GCGTGTGACCAGCGTGTGTGCATCCCGGTGTACAGAGCACGGAACCTGTAAAGATGGG 2433
 QUERY: 2506 AAATGTGAATGCCGAGAGGGCTGGAATGGTGAACACTGCACCATTGGTAGGCAAACGGCA 2565

SBJCT: 2434 AAATGTGAATGCAGAGAGGGCTGGAATGGGGAGCACTGCACCATTGGTAGGCAAACGACA 2493
 QUERY: 2566 GGCACCAGAAACAGATGGCTGCCCTGACTTGTGCAACGGTAACGGGAGATGCACACTGGGT 2625
 |||||
 SBJCT: 2494 GGCACCAGAAACAGATGGCTGCCCTGACTTGTGCAATGGCAACGGGAGGTGCACGCTGGGC 2553
 QUERY: 2626 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCCGGATGCAACGTTGCC 2685
 |||||
 SBJCT: 2554 CAGAACAGCTGGCAGTGTGTCTGCCAGACCGGCTGGAGAGGGCCTGGATGCAACGTTGCC 2613
 QUERY: 2686 ATGGAAACTTCTGTGCTGATAACAAGGATAATGAGGGAGATGGCTGGTGGATTGTTTG 2745
 |||||
 SBJCT: 2614 ATGGAAACCTCTGTGCCGATAACAAGGATAACGAGGGAGATGGCTTGGTTGACTGCCTA 2673
 QUERY: 2746 GACCCCTGACTGCTGCCTGCAGTCAGCCTGTGAGAACAGCCTGCTCTGCCGGGGTCCCGG 2805
 |||||
 SBJCT: 2674 GTCCAGATTGCTGCCTCCAGTCCACTTGTCAAAACAGCCTGCTGTGCCGGGGTCCCGC 2733
 QUERY: 2806 GACCCACTGGACATCATTCAGCAGGGCCAGACGGATTGGCCCGCAGTGAAGTCCTTCTAT 2865
 |||||
 SBJCT: 2734 GATCCTCTTGACATCATACACAGAGCCATTCTGGTTACCAGCTGTGAAGTCATTCTAT 2793
 QUERY: 2866 GACCGTATCAAGCTCTTGGCAGGCAAGGATAGCACCCACATCATTCCTGGAGAGAACCT 2925
 |||||
 SBJCT: 2794 GATCGAATCAAGCTCTTAGTGGGAAGGACAGCACTCATATCATTCAGGAGAAAATCCC 2853
 QUERY: 2926 TTCAACAGCAGCTTGGTTTCTCTCATCCGAGGCCAAGTAGTAACACAGATGGAACCTCC 2985
 |||||
 SBJCT: 2854 TTCAACAGCAGCCTTGTGTCTCTTATAAGAGGCCAAGTGGTGACTACAGATGGAACGCT 2913
 QUERY: 2986 CTGGTCGGTGTGAACGTGTCTTTTGTCAAGTACCCAAAATACGGCTACACCATCACCCGC 3045
 |||||
 SBJCT: 2914 CTAGTTGGGGTCAACGTGTCTTTTGTCAAGTATCCAAAGTATGGCTATACCATCACTCGT 2973
 QUERY: 3046 CAGGATGGCACGTTTCGACCTGATCGCAAATGGAGGTGCTTCCTTGACTCTACACTTTGAG 3105
 |||||
 SBJCT: 2974 CAGGATGGCATGTTTGACTTGGTTGTCAACGGTGGATCATCCCTAACTTTGCACCTTGAA 3033
 QUERY: 3106 CGAGCCCCGTTTCATGAGCCAGGAGCGCACTGTGTGGCTGCCGTGGAACAGCTTTTACGCC 3165
 |||||
 SBJCT: 3034 CGGGCCCCATTTATGAGTCAGGAAAGGACAGTATGGCTGCCGTGGAACAGCTTCTATGCC 3093
 QUERY: 3166 ATGGACACCCTGGTGTGAAGACCGAGGAGAACTCCATCCCCAGCTGTGACCTCAGTGGC 3225
 |||||
 SBJCT: 3094 ATGGACACGCTTGTAATGAAAACAGAGGAGAACTCCATTCCCAGCTGTGATCTCAGTGGC 3153
 QUERY: 3226 TTTGTCCGGCCTGATCCAATCATCATCTCCTCCCCACTGTCCACCTTCTTTAGTGCTGCC 3285
 |||||
 SBJCT: 3154 TTTGTGAGACCTGATCCAGTCATATTTATCACCAGTGTCAACTTTCTTCAGTGATGCT 3213
 QUERY: 3286 CCTGGGCAGAAATCCCATCGTGCCTGAGACCCAGGTTCTTCATGAAGAAATCGAGCTCCCT 3345
 |||||
 SBJCT: 3214 CCTGGCCGAAATCCTATTGTACCAGAAACCCAGGTTCTTCATGAAGAAATTGAGGTCCT 3273
 QUERY: 3346 GG 3347
 ||
 SBJCT: 3274 GG 3275
 SCORE = 547 BITS (276), EXPECT = E-152
 IDENTITIES = 540/628 (85%)
 STRAND = PLUS / PLUS
 QUERY: 782 GTCGTCCCATTCACCTACATCCTCGCCTAGTCTCCTCCCATCTGCTCAGCTGCCTAGCT 841
 |||||
 SBJCT: 587 GTCGTCCCATTCACCTACATCCTCGTCTAGCCTTCTCCCATCTGCTCAGCTGCCAGTT 646
 QUERY: 842 CCCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAACACCTCCCATC 901

SBJCT: 647 CTCATAATCCTCCACCAGTTAGCTGCCAGATGCCATTGCTAGACAGCAATACGTCCCATC 706
 QUERY: 902 AAATCATGGACACCAACCCCTGATGAGGAATTCTCCCCAATTCATACCTGCTCAGAGCAT 961
 SBJCT: 707 AAATCATGGACACCAATCCTGACGAGGAGTTCTCTCCTAATTCATACCTACTAAGAGCAT 766
 QUERY: 962 GCTCAGGGCCCCAGCAAGCCTCCAGCAGTGGCCCTCCGAACCACCACAGCCAGTCGACTC 1021
 SBJCT: 767 GTTCAGGGCCACAGCAGGCATCCAGCAGTGGCCCTTCAAACCATCACAGCCAGTCAACGC 826
 QUERY: 1022 TGAGGGCCCCCTCTCCACCCCCCTCACAACCACACGCTGTCCCATCACCCTCGTCCGCCA 1081
 SBJCT: 827 TGAGGGCCACCTCTCCCCCTCCTCACAACCCTCGCTGTCCCATCATCACTCGTCTGCCA 886
 QUERY: 1082 ACTCCCTCAACAGGAACTCACTGACCAATCGGCGGAGTCAGATCCACGCCCCGGCCCCAG 1141
 SBJCT: 887 ACTCCCTCAACAGGAACTCGCTCACCAACCGCGCAACCAGATCCACGCGCCTGCTCCCG 946
 QUERY: 1142 CGCCCAATGACCTGGCCACCACACCAGAGTCCGTTAGCTTCAGGACAGCTGGGTGCTAA 1201
 SBJCT: 947 CTCCCAATGACCTGGCGACCACGCCTGAGTCTGTGCAGCTGCAGGACAGCTGGGTGCTCA 1006
 QUERY: 1202 ACAGCAACGTGCCACTGGAGACCCGGCACTTCTCTTCAAGACCTCCTCGGGAGCACAC 1261
 SBJCT: 1007 ACAGCAACGTGCCGCTGGAGACCAGGCATTTCTTGTTTAAGACATCTTCTGGAACGACTC 1066
 QUERY: 1262 CCTTGTTTCAGCAGCTCTTCCCCGGGATACCCTTTGACCTCAGGAACGGTTTACACGCCCC 1321
 SBJCT: 1067 CGCTGTTTCAGTAGCTCTTCCCCTGGCTACCCACTGACCTCAGGAACAGTTTATACTCCAC 1126
 QUERY: 1322 CGCCCCGCTGTGTCAGGAATACTTTCTCAGGAAGGCTTTCAAGCTGAAGAAGCCCT 1381
 SBJCT: 1127 CTCCCAGGCTGTTACCTAGAAATACATTTTCCAGGAATGCATTCAGCTGAAAAGCCCT 1186
 QUERY: 1382 CCAAATACTGCAGCTGGAAATGTGCTGC 1409
 SBJCT: 1187 CCAAGTATTGTAGCTGGAAATGTGCTGC 1214
 SCORE = 391 BITS (197), EXPECT = E-105
 IDENTITIES = 593/725 (81%)
 STRAND = PLUS / PLUS
 QUERY: 7156 CATGTCTACAATCACTCCAACCTCGGAGATTACCTCACTGTACTACGACCTCCAGGGCCAC 7215
 SBJCT: 7084 CATGTCTACAATCATTCCAATTGAGAAATTACCTCTCTGTATTATGATCTGCAAGGCCAC 7143
 QUERY: 7216 CTCTTTGCCATGGAGAGCAGCAGTGGGGAGGAGTACTATGTTGCCTCTGATAACACAGGG 7275
 SBJCT: 7144 CTCTTTGCAATGGAGAGTAGCAGTGGGGAAGAATATTATGTCGCCTCCGATAACACGGGC 7203
 QUERY: 7276 ACTCCTCTGGCTGTGTTTCAGCATCAACGGCCTCATGATCAAACAGCTGCAGTACACGGCC 7335
 SBJCT: 7204 ACTCCGCTAGCCGTATTTCAGCATCAATGGCCTCATGATCAAACAGCTTCAGTACACTGCA 7263
 QUERY: 7336 TATGGGGAGATTTATTATGACTCCAACCCCGACTTCCAGATGGTCATTGGCTTCCATGGG 7395
 SBJCT: 7264 TACGGAGAGATTTATTATGACTCAAACCCTGATTTCCAGCTGGTTATTGGGTTCCATGGA 7323
 QUERY: 7396 GGACTCTATGACCCCTGACCAAGCTGGTCCACTTCACTCAGCGTGATTATGATGTGCTG 7455
 SBJCT: 7324 GGGCTGTATGATCCTTTAACCAAACTCGTCCATTTTACCCAAGGGACTACGATGTCCCTT 7383
 QUERY: 7456 GCAGGACGATGGACCTCCCCAGACTATACCATGTGGAAAAACGTGGGCAAGGAGCCGGCC 7515
 SBJCT: 7384 GCTGGACGCTGGACATCTCCTGATTACAAATGTGGAAAAACATTGGTAGAGAACCTGCT 7443
 QUERY: 7516 CCGTTTAACTGTATATGTTCAAGAGCAACAATCCTCTCAGCAGTGAGCTAGATTGTAAG 7575

IDENTITIES = 397/475 (83%)
STRAND = PLUS / PLUS

```
5  QUERY: 299 GACACCGCTCTTTGACCAGAGGACGCTGTGGCAAAGAGTGTGCTACACAAGCTCCTCTC 358
    ||||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
   SBJCT: 20  GACACCGCTCTTTGACGAGAGGCCGGTGCAGGAAGGAGTGTGCTATACTAGTTCTTCAC 79

    QUERY: 359 TGGACAGTGAGGACTGCCGGGTGCCCACACAGAAATCCTACAGCTCCAGTGAGACTCTGA 418
    ||||||| |||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
   SBJCT: 80  TCGACAGTGAAGACTGCAGAGTACCAGCTCAGAAGTCCTACAGCTCCAGTGAGACCCCTGA 139

    QUERY: 419 AGGCCTATGACCATGACAGCAGGATGCACTATGGAAACCGAGTCACAGACCTCATCCACC 478
    || ||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 140 AAGCATATGGCCATGACACGAGGATGCACTACGAAATCGAGTTTCAGACCTGGTTCACA 199

    QUERY: 479 GGGAGTCAGATGAGTTTCTAGACAAGGAACCAACTTCACCTTGCCGAAGTGGGCATCT 538
    ||||||| ||||||| ||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 200 GGGAGTCGATGAGTTTCCAAGGCAAGGAACGAACCTTCACCTTGCCGAAGTGGGAATCT 259

    QUERY: 539 GTGAGCCCTCCCCACACCGAAGCGGCTACTGCTCCGACATGGGGATCCTTCACCAGGGCT 598
    ||||||| ||||||| ||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 260 GTGAGCCCTCTCCCATCGAAGTGGCTACTGCTCGGACATAGGAATACTCCATCAAGGCT 319

    QUERY: 599 ACTCCCTTAGCACAGGGTCTGACGCCGACTCCGACACCGAGGGAGGGATGTCTCCAGAAC 658
    || ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
   SBJCT: 320 ATTCTTTGACCACTGGCTCTGATGCTGACTCAGACACGGAGGGCGGGATGTCTCCAGAGC 379

    QUERY: 659 ACGCCATCAGACTGTGGGGCAGAGGGATAAAATCCAGGCGCAGTTCCGGCCTGTCCAGTC 718
    ||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 380 ACGCGATCAGGCTGTGGGGAAGAGGGATCAAATCCAGCCGAAGTTCTGGCCTGTCAAGTC 439

    QUERY: 719 GTGAAAACCTCGGCCCTTACCCTGACTGACTCTGACAACGAAAACAAATCAGATGA 773
    ||||||| ||||||| || ||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 440 GTGAAAACCTCGGCTCTCACGCTCACTGACTCCGACAATGAGAACAAGTCAGATGA 494
```

The full FCTR3a amino acid sequence also has 342 of 383 amino acid residues (89%) identical to, and 342 of 383 residues (89%) positive with, the 276 amino acid residue Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc: NP_035986.2) (SEQ ID NO:68) (Table 3P).

Table 3P. BLASTP of FCTR3a against Odd Oz/ten-m homolog 2 - (SEQ ID NO:68)

>GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M
HOMOLOG 3

(DROSOPHILA) [MUS MUSCULUS]

GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]

LENGTH = 2764

SCORE = 495 BITS (1274), EXPECT = E-139

IDENTITIES = 342/383 (89%), POSITIVES = 342/383 (89%), GAPS = 41/383 (10%)

```
50  QUERY: 37  HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 96
    ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 189 HNPPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTL 248

    QUERY: 97  RPPLPPPHNHTLSHHSSANSLSNRSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 156
    ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 249 RPPLPPPHNHTLSHHSSANSLSNRSLTNRRSQIHAPAPAPNDLATTPESVQLQDSWVLN 308

    QUERY: 157 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 216
    ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||
   SBJCT: 309 SNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRKAFKLKKPS 368
```

QUERY: 217 KYCSWKCAALSAIAAALLLAILLAYFI----- 243
 ||||||||||||||||||
 SBJCT: 369 KYCSWKCAALSAIAAALLLAILLAYFIAMHLLGLNWQLPADGHTFNNGVRTGLPGNDDV 428

 5 QUERY: 244 -----VPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 295
 ||||||||||||||||||
 SBJCT: 429 ATPVSGGKVPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLKFNISLGKD 488

 10 QUERY: 296 ALFGVYIRRLPSPHAQYDFMERLDGKEKWSVSPRERRSIQTLVQNEAVFVQYLDVGL 355
 ||||||||||||||||||
 SBJCT: 489 ALFGVYIRRLPSPHAQYDFMERLDGKEKWSVSPRERRSIQTLVQNEAVFVQYLDVGL 548

 QUERY: 356 WHLAFYNDGKDKEMVSFNTVVLD 378
 ||||||||||||||||||
 15 SBJCT: 549 WHLAFYNDGKDKEMVSFNTVVLD 571

The full FCTR3b amino acid sequence has 2442 of 2802 amino acid residues (87%) identical to, and 2532 of 2802 residues (90%) positive with, the 2802 amino acid residue teneurin-2 [*Gallus gallus*] (GenBank Acc: AJ279031) (SEQ ID NO:69) (Table 3Q).

Table 3Q. BLASTP of FCTR3a against Teneurin-2 - (SEQ ID NO:69)

>GI|10241574|EMBL|CAC09416.1| (AJ279031) TENEURIN-2 [GALLUS GALLUS]
 LENGTH = 2802

 SCORE = 4853 BITS (12589), EXPECT = 0.0
 IDENTITIES = 2510/2802 (87%), POSITIVES = 2600/2802 (90%), GAPS = 69/2802 (2%)

 QUERY: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSDRMHYGNR 60
 ||+|||||||||||||||||||||||||||||||||||+||||||
 SBJCT: 1 MDIKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPAQKSYSSSETLKAYGHDTRMHYGNR 60

 30 QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120
 ||+||+|||||||||||||||||||||||||||||||||||+||||||||||||||||||
 SBJCT: 61 VSDLVHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120

 35 QUERY: 121 GGMSPEHAIRLWGRGIKSRSSSGLSSRENSALTLTDSNENKSDDENG----- 168
 ||||||||||||||||||||||||||||||||||||||||
 SBJCT: 121 GGMSPEHAIRLWGRGIKSSRSSSGLSSRENSALTLTDSNENKSDDENGFHTLSEKLDKDR 180

 40 QUERY: 169 -----RPIPTSSPSSLPSAQLPSSHNPVSCQMPLLDSNTSHQIMDT 212
 ||||||||| ||||||||||||||||||||||||||||||||
 SBJCT: 181 QTSWQQLAETKNSLIRRPPTSSSLLPSAQLPSSHNPVSCQMPLLDSNTSHQIMDT 240

 45 QUERY: 213 NPDEEFSPNSYLLRACSGPQQASSSGPPNHHSQSTLRPPLPPPHNHTLSHHHSSANSINR 272
 ||||||||||||||||||||||||||||||||||||||||
 SBJCT: 241 NPDEEFSPNSYLLRACSGPQQASSSGPSNHHSQSTLRPPLPPPHNHTLSHHHSSANSINR 300

 50 QUERY: 273 XXXXXXXXQIHAPAPAPNDLATTPEVQLQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXX 332
 ||||||||||||||||||||||||||||||||||||
 SBJCT: 301 NSLTNRRNQIHAPAPAPNDLATTPEVQLQDSWVLNSNVPLETRHFLFKTSSGTTPLFSS 360

 55 QUERY: 333 XXXXYPLTSGTVYTPPPRLLPRNTFSRKAFKLKPSKYCSWKCKXXXXXXXXXXXXXXXX 392
 ||||||||||||||||||||||||||||||||||||
 SBJCT: 361 SSPGYPLTSGTVYTPPPRLLPRNTFSRNFKLKPSKYCSWKCAALSAIAAAVLLAILLA 420

 60 QUERY: 393 YFIV-----PWSLKNSSIDSGEAE 411
 ||| ||| +|||||||
 SBJCT: 421 YFIAMHLLGLNWQLPADGHTFSNGLRPGAAGAEDGAAAPPAGRGFVWTRNSSIDSGETE 480

 QUERY: 412 VGRRTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRLPSPHAQYDFMERL 471
 |||+||||||||||||||||||||||||||||||||||
 SBJCT: 481 VGRKVTQEVPPGVFWRSQIHISQPQFLKFNISLGKDALFGVYIRRLPSPHAQYDFMERL 540

QUERY: 472	DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEVVSFNTVVLDS	531
SBJCT: 541	DGKEKWSVVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYNDGKDKEVVSFNTVVLDS	600
QUERY: 532	VQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCCQYSGWKGAEE	591
SBJCT: 601	VQDCPRNCHGNGECVSGVCHCFPGFLGADCAKAACPVLCSGNGQYSKGTCLCYSGWKGP	660
QUERY: 592	CDVPMNQCIDPSCGGHGSICIDGNCVCSAGYKGEHCEEVDCLDPTCSSHGVCVNGECLCSP	651
SBJCT: 661	CDVPISQCIDPSCGGHGSIEGNCVCSIGYKGENCEEVDCLDPTCSNHGVCVNGECLCSP	720
QUERY: 652	GWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMPDCSVEVCSVDGTHGVCIGG	711
SBJCT: 721	GWGGINCELPRAQCPDQCSGHGTYLSDTGLCSCDPNWMPDCSVEVCSVDGTHGVCIGG	780
QUERY: 712	ACRCEEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHCTIGRQTAGTETDGC	771
SBJCT: 781	ACRCEEGWTGVACDQRVCHPRCTEHGTCKDGKCECREGWNGEHCTIGRQTTGTETDGC	840
QUERY: 772	LCNNGNRCTLGQNSWQCVCQGTGWRGPGCNVAMETSCADNKDNEGDLVDCLPDCCQLQA	831
SBJCT: 841	LCNNGNRCTLGQNSWQCVCQGTGWRGPGCNVAMETSCADNKDNEGDLVDCLPDCCQLQ	900
QUERY: 832	CQNSLLCRGSRDPLDIIQQGQTDWPAVKSFYDRIKLLAGKDSTHIIIPGENPFNSSLVSLI	891
SBJCT: 901	CQNSLLCRGSRDPLDIIQQSHSGSPAVKSFYDRIKLLVGKDSTHIIIPGENPFNSSLVSLI	960
QUERY: 892	RGQVVTTDGTPLVGVNVSVFKYPKYGYTITRQDGTFDLIANGGASLTLHFERAPFMSQER	951
SBJCT: 961	RGQVVTTDGTPLVGVNVSVFKYPKYGYTITRQDGMFDLVANGSSLTLHFERAPFMSQER	1020
QUERY: 952	TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPPIIISSPLSTFFSAAPQNPIVPE	1011
SBJCT: 1021	TVWLPWNSFYAMDTLVMKTEENSIPSCDLSGFVRPDPVPIISSPLSTFFSDAPGRNPIVPE	1080
QUERY: 1012	TQVLHEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLIRVHLMVAVEGHLFQK	1071
SBJCT: 1081	TQVLHEEIEVPGSSIKLIYLSSRTAGYKSLKIIMTQSLVPLNLIKVHLMVAVEGHLFQK	1140
QUERY: 1072	SFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELD	1131
SBJCT: 1141	SFLASPNLAYTFIWDKTDAYGQKVYGLSDAVVSVGFYETCPSLILWEKRTALLQGFELD	1200
QUERY: 1132	PSNLGGWSLDKHHILNVKSGILHKGTEGENQFLTQQPAIITSIMGNRRRSISCPSCNGLA	1191
SBJCT: 1201	PSNLGGWSLDKHHVILNVKSGILHKGNGENQFLTQQPAVITSIMGNRRRSISCPSCNGLA	1260
QUERY: 1192	EGNKLLAPVALAVGIDGSLYVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA	1251
SBJCT: 1261	EGNKLLAPVALAVGIDGSLFVGDFNYIRRIFPSRNVTSILELRNKEFKHSNNPAHKYYLA	1320
QUERY: 1252	VDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCLPFDEARCGDGGKAID	1311
SBJCT: 1321	VDPVSGSLYVSDTNSRRIYKVKSLTGTDLAGNSEVVAGTGEQCLPFDEARCGDGGKAVD	1380
QUERY: 1312	ATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVAQV	1371
SBJCT: 1381	ATLMSPRGIAVDKYGLMYFVDATMIRKVDQNGIISTLLGSNDLTAVRPLSCDSSMDVSVQ	1440
QUERY: 1372	RLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQVPGIDYSLSKXXXXX	1431
SBJCT: 1441	RLEWPTDLAVDPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQVPGIDYSLSKLAIHS	1500
QUERY: 1432	XXXXXXXXXXXXXGVLVYITETDEKKINRLRQVTTNGEICLLAGAASXXXXXXXXXXXXXYS	1491
SBJCT: 1501	ALESASAIASHTGVLVYISETDEKKINRLRQVTTNGEICLLAGAASDCCKNDVNCNCYS	1560

QUERY: 2512 IREKAGHWFATTTPIIGKGIMFAIKEGRVTTGVSSIASEDSRKVASVLNNAYYLDKMHYS 2571
 |||||+|||||+|||+|||++|||+|||+|||+|||+|||
 SBJCT: 2581 IREKAGHWFATSTPIIGKGIMFAVKKGRVTTGISSIATDDSRKIASVLNSAHYLEKMHYS 2640
 5 QUERY: 2572 IEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLLVNGRTRRFTNIEFQY 2631
 |||||+|||||+|||||+|||||+|||||+|||||+|||||+|||||
 SBJCT: 2641 IEGKDTHYFVKIGSADSDVTLAMTSGRKVLDSGVNVTVSQPTLLINGRTRRFTNIEFQY 2700
 10 QUERY: 2632 STLLLSIRYGLTPDTLDEEKARVLDQARQALGTAWAKEQQKARDGREGSRLWTEGEKQQ 2691
 |||++||| |||||+|||||+|||||+|||||+|||||+|||||
 SBJCT: 2701 STLLINIRYGLTADTLDEEKARVLDQARQALGSAWAKEQQKARDGREGSRVWTDGEKQQ 2760
 QUERY: 2692 LLSTGRVQYEGYYVLPVEQYPELADSSSNIQFLRQNEGMKR 2733
 ||+|||||+|||||+|||||+|||||+|||||+|||||+|||||
 15 SBJCT: 2761 LLNTGRVQYEGYYVLPVEQYPELADSSSNIQFLRQNEGMKR 2802

The FCCTR3bcde and f amino acid sequences have 1524 of 2352 amino acid residues
 (64%) identical to, and 1881 of 2532 residues (79%) positive with, the amino acid residues
 429-2771, 93 of 157 residues (59%) identical to and 118 of 157 residues (74%) positive with
 20 amino acid residues 1-155, and 59 of 152 residues (38%) identical to and 68 of 152 residues
 (43%) positive with amino acid residues 211-361 of Ten-m4 [*Mus musculus*] (ptnr: GenBank
 Acc: BAA77399.1) (SEQ ID NO:70) (Table 3R).

**Table 3R. BLASTP of FCCTR3b, c, d, e, and f against *Mus musculus* Ten-m4 - (SEQ ID
 NO:70)**

25 >GI|4760782|DBJ|BAA77399.1| (AB025413) TEN-M4 [MUS MUSCULUS]
 LENGTH = 2771
 SCORE = 3089 BITS (8008), EXPECT = 0.0
 30 IDENTITIES = 1524/2352 (64%), POSITIVES = 1881/2352 (79%), GAPS = 28/2352 (1%)
 QUERY: 401 KNSSIDSGEAEVGRVTVQVPPGVFWRSQIHISQPQFLKFNISLKGKDALFGVYIRRLGPP 460
 ++| |||| +||| +|++|| ||||+ | | |||+||| || |+| |+|||
 35 SBJCT: 429 EDSFIDSGEIDVGRRASQKIPPGTFWRSQVFDHPVHLKFENVSLGKAALVGIYGRKGLPP 488
 QUERY: 461 SHAQYDFMERLDGK-----EKSVSVESPRERRSIQTLVQNEAVFVQYLDVGLWHLAFYND 515
 || |+|+| |||+ | |+ | + | |+| || |+||| |+||| |||
 SBJCT: 489 SHTQFDFVELLDGRRLLTQEARSLGEPQRQSRGPVPPSSHETGFIQYLDSGIWHLAFYND 548
 40 QUERY: 516 GKDKEMVSFNTVVLDSVQDCPRNCHGNCEVSGVCHCFPGFLGADCAKACPVLCSGNGQ 575
 ||+ |+||| ++|| +| |+|||++|| |||| ||| ++|+||| |||
 SBJCT: 549 GKESVVSFLTTAIESVDNCPNCGNGDCISGTCHCFLGFLGPDGCRASCPVLCSGNGQ 608
 45 QUERY: 576 YSKGTCQCYSGWKGAECVPMNQCIDPSCGGHSGCIDGNCVCSAGYKGEHCEEVDCLDPT 635
 || |+|+||| ||||| |||| +| |+|| |+|+ |||| |||||+|||
 SBJCT: 609 YMKGRCLCHSGWKGAECVPTNQCIDVACSSHGTCIMGTICINPGYKGESCEEVD CMDPT 668
 QUERY: 636 CSSHGVCVNCECLSPGWGGLNCELARVQCPDQCSGHGTYLPDTGLCSCDPNWMGPDCSV 695
 ||| |||| ||| || |||| ||| | |||||+||| |||+||| |||+
 50 SBJCT: 669 CSSRGVCVRGECHCSVGWGGTNCETPRATCLDQCSGHGTYLPDTGLCNCDPSTGHDCSI 728
 QUERY: 696 EVCSVDCGTHGVCIGGACRCBEGWTGAACDQRVCHPRCIEHGTCKDGKCECREGWNGEHC 755
 |+|+ ||| ||||+|| ||||+|| ||||| ||||| |||||+||| |||||
 55 SBJCT: 729 ETCAADCGHGVCGGTCTCRCDGWMGAACDQACHPRCAEHGTCTRDGKCECSPGWNGEHC 788

 QUERY: 756 TIGRQTAGTETDGCPLDNGNGRCTLGQNSWQCVCQTGWRGPGCNVAMETSCADNKDNEG 815
 || |+|| ||||| ||| |||| |||| |||+ +||| |||+|||
 SBJCT: 789 TIAHYLDRVVKEGCPGLCNGNGRCTLDLNGWHCVCQLGWRGTGCDTSMETGCGDGKDNNDG 848

QUERY: 816 DGLVDCLDPCCLQSACQNSLLCRGSRDPLDIIQOGQT--DWPVKSFYDRIKLLAGKDS 873
 SBJCT: 849 DGLVDCMDPCCLQPLCHVNPLCLGSPDPLDIIQETQAPVSQQNLNPFYDRIKFLVGRDS 908
 5 QUERY: 874 THIIPGENPFNSLVSIRGQVVTDDGTPLVGVNVSFVKYPKYGYTITRQDGTDFDLIANG 933
 SBJCT: 909 THSIPGENPFDGGHACVIRGQVMTSDGTPLVGVNISFINNPLFGYTISRQDGSFDFLTNG 968
 10 QUERY: 934 GASLTLHFERAPFMSQERTVWLPWNVSFYAMDTLVMKTEENSIPSCDLSGFVRPDPIISS 993
 SBJCT: 969 GISILRFRERAPFITQEHTLWLPWDRFVFMETIVMRHEENEIPSCDLSNFARPNPVVSPS 1028
 QUERY: 994 PLSTFFSAAPGQNPIVETQVLHEEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPL 1053
 15 SBJCT: 1029 PLTSFASSCAEKGPVPEIQALQEEIIVAGCKMRLSYLSSRTPGYKSVLRISLTHPTIPF 1088
 QUERY: 1054 NLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVVSVGFYETCP 1113
 SBJCT: 1089 NLMKVHLMVAVEGRLFRKWFAAAPDLSEYFIWDKTDVYNQKVFGEAFVSVGYEYESCP 1148
 20 QUERY: 1114 SLILWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKTGENQFLTQQPAIITSI 1173
 SBJCT: 1149 DLILWEKRTAVLQGYEIDASKLGGWSLDKHHALNIQSGILHKGNGENQFVSQQPPVIGSI 1208
 25 QUERY: 1174 MGNGRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRIRFPSRNVTSILEL 1233
 SBJCT: 1209 MGNGRRRSISCPSCNGLADGNKLLAPVALTCGSDGSLYVGDFNYIRIRFPSGNVTNILEM 1268
 30 QUERY: 1234 RNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGE 1293
 SBJCT: 1269 RNKDFRHSHPAHKYYLATDPMGAVFLSDTNSRRVFKVKSTTVVKDLVKNSEVVAGTGD 1328
 QUERY: 1294 QCLPFDEARCGDGGKKAIDATILMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSND 1353
 35 SBJCT: 1329 QCLPFDDTRCGDGGKATEATLTNPRGITVDKFLIYFVDGTMIRRVQDNGIISTLLGSND 1388
 QUERY: 1354 LTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNLSLYLENNVILRITENHQVSIAGRPM 1413
 SBJCT: 1389 LTSARPLSCDSVMEISQVRLEWPTDLAINPMDNLSLYLDNNVVLQISENHQVRIVAGRPM 1448
 40 QUERY: 1414 HCQVPGID-YSLSKXXXXXXXXXXXXXXXXXGVLVYITETDEKKINRLRQVTTNGEICLL 1472
 SBJCT: 1449 HCQVPGIDHFLLSKVAIHATLESATALAVSHNGVLYIAETDEKKINRIRQVTTSGEISLV 1508
 45 QUERY: 1473 AGAASXXXXXXXXXXYSGD DAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKN 1532
 SBJCT: 1509 AGAPSGCDCKNDANCDGSGDDGYAKDAKLTNPSSLAVCADGELYVADLGNIRIRFIRKN 1568
 50 QUERY: 1533 KPVLNAFNQYEAASPEQELVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTTELIDNNG 1592
 SBJCT: 1569 KPFLNTQNMIELSSPIDQELYLFDTSKGHLYTQSLPTGDYLYNFTYTGDGDITHITDNNG 1628
 QUERY: 1593 NSLKIRRDSSGMPRHLLMPDNQIITLVGTNGGLKVVSTQNLGLMITYDGTGLLATKS 1652
 55 SBJCT: 1629 NMVNVRDSTGMPLWLVPDQGVYVWVTMGINSALRSVTTQGHELAMMTYHGNSGLLATKS 1688
 QUERY: 1653 DETGWTTTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNRDDVTITNLSSV 1712
 SBJCT: 1689 NENGWTTTFEYDSFGRLTNVTFPTGQVSSFRSDTSSVHVQVETSSK-DDVTITTNLSAS 1747
 60 QUERY: 1713 EASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSSEPHVLAGTITPTIGRCNISLPE 1772
 SBJCT: 1748 GAFYTLQDQVRNSYIIGADGSLRLLLANGMEVALQTEPHLLAGTVNPTVGKRVNLTLPID 1807
 65 QUERY: 1773 NGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLRILY 1832
 SBJCT: 1808 NGLNLVEWRQRKEQARGQVTVFGRRLRVHNRNLLSLDFDRVTRTEKIYDDHRKFTLRILY 1867

QUERY: 1833 DQVGRPFLWLPSSGLAAVNVSYFFNGRLAGLQRGAMSERTDIDKQGRIVSRMFADGKVWS 1892
 || ||| || ||| | |||+ | +||+|| ||| + |+ ||| ||+|||+||
 SBJCT: 1868 DQAGRPSLWSPSSRLNGVNVITYSPGGHIAGIQRGIMSERMEYDQAGRITSRIFADGKMWS 1927

 5 QUERY: 1893 YSYLDKSMVLLQSQRYIFEYDSSDRLLAVTMPSPVARHSMSTHTSIGYIRNIYNPPESN 1952
 |+|+||| || |||||+| +||| +|||+||| ++ | |+| ||| ||| |
 SBJCT: 1928 YTYLEKSMVLHLHSQRQYIFEFDKNDRLSSVTMPNVARQTLETIRSVGYRNIYQPPEGN 1987

 10 QUERY: 1953 ASVIFDYSDDGRIKTSFLGTGRQVFKYKGLSKLSEIVYDSTAVTFGYDETTGVLKMVN 2012
 ||| |+++| +| | +|||+| |||||+| +||+| |+| ||| |+|| ||
 SBJCT: 1988 ASVIQDFTEDGHLHTFYLGTGRVVIKYKGLSKLAETLYDTTKVSFTYDETAGMLKTVN 2047

 QUERY: 2013 LQSGGFSCITIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLP 2072
 ||+ ||+|||+|||+||+||+||+||| |||||+ ||+ ||+|||
 15 SBJCT: 2048 LQNEGFTCTIRYRQIGPLIDRQIFRTEEGMVNARFDYNY-DNSFRVTSMQAVINETPLP 2106

 QUERY: 2073 VDLYRYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRIKEVQYEMFRSLMY 2132
 +|||+||+|| | |||||+|||+|||+|||+|||+|||+|||+|||+|||
 20 SBJCT: 2107 IDLYRYDDVSGKTEQFGKFGVIYYDINQIITAVMTLTKHFDAYGRMKVQYEIFRSLMY 2166

 QUERY: 2133 WMTVQYDSMGRVIKRELKGPYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSDXXXXX 2192
 |||||+|||+||+||+|||+||+||+||| |||||+||+||+||| |||||
 SBJCT: 2167 WMTVQYDNMGRVVKELKGPYANTTRYSEYDADGQLQTVSINDKPLWRYSYDLNGLNH 2226

 25 QUERY: 2193 XXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKA 2252
 | || |||||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||
 SBJCT: 2227 LLSPGNSARLTPLRYDLRDRITRLGDVQYKMDDEGFLRQGGDVFEYNSAGLLIKAYNRA 2286

 QUERY: 2253 SGWSVQYRYDGVGRASYKTNLGHHLQYFYSDLHNPTRITHVYNHNSSEITSLYYDLQGH 2312
 |||||+|||+||| | ++ |||+||+|| ||++||+|||+|||+|||+|||
 30 SBJCT: 2287 SGWSVRYRYDGLGRRVSSKSSHHLQFFYADLTNPTKVTHLYNHSSSEITSLYYDLQGH 2346

 QUERY: 2313 LFAMESSSGEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHG 2372
 ||||| |||+||+|| | || ||||| |||||+ ||||| |||+||+||+|||
 35 SBJCT: 2347 LFAMELSSGDEFYIACDNIGTPLAVFSGTGLMIKQILYTAYGEIYMDTNPNFQIIIGYHG 2406

 QUERY: 2373 GLYDPLTKLVHFTQRDYLVDLAGRWTSPTYTMWKNVGKEP-APFNLYMFKSNNPLSSELDL 2431
 |||||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||
 40 SBJCT: 2407 GLYDPLTKLVHMGRRDYDVLAGRWTSPDHELWKRLSSNSIVPFHLYMFKNPNPISNSQDI 2466

 QUERY: 2432 KNYVTDVKSWSLVMFGQLSNIIPGFPRAKMYFVPPPYELSESQAS---ENGQLITGVQQ 2487
 | ++||| |||+ |||| | +||+||+ | + ||| +| + | |||
 SBJCT: 2467 KCFMTDVNSWLLTFGFQLHNVIPGYPKPDTDAMEPSYELVHTQMKTEWDNKSILGVQC 2526

 45 QUERY: 2488 TTERHNQAFMALE-----GQVITKKLHASIREKAGHWFATTTPIIGKIMFAIKEGRVT 2541
 ++ +||+ || | | | +| |||+ |||+ |||+ |||+ |||+ |||+ |||
 SBJCT: 2527 EVQKQLKAFVTLERFDQLYGSTITSCQAPETKK---FASSGSIFGKGVKFALKDGRVT 2582

 QUERY: 2542 TGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGRKV 2601
 | + |+||| |||+||+|||+||+ +||+||+ ||||| || ++||| || + ||+
 50 SBJCT: 2583 TDIISVANEDGRRIAAILNNAHYLENLHFTIDGVDTHYFVKPGPSEGDLAILGLSGGRRT 2642

 QUERY: 2602 LESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQARQR 2661
 ||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||+|||
 55 SBJCT: 2643 LENGVNVTVSQINTMLSGRTRRYTDIQLQYRALCLNTRYG---TTVDEEKVRVLELARQR 2699

 QUERY: 2662 ALGTAWAKEQQKARDGREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSN 2721
 |+ |||+|||+ |+| || | ||+|||+||+|||+||+|||+|||+|||+|||+|||
 60 SBJCT: 2700 AVRQAWAREQQRLREGEEGLRAWTDGEKQVLTNTRGVQGYDGFVTSVEQYPELSDSANN 2759

 QUERY: 2722 IQFLRQNEGMGR 2733
 | |+||+|||+|||
 SBJCT: 2760 IHFMRQSEMGR 2771

 65 SCORE = 161 BITS (407), EXPECT = 2E-37
 IDENTITIES = 93/157 (59%), POSITIVES = 118/157 (74%), GAPS = 4/157 (2%)
 QUERY: 1 MDVKDRR-HRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGN 59

SBJCT: 1 MDVKERKPYRSLTRRR-DAERRYTSSSADSEEGKGP-QKSYSSSETLKAYDQDARLAYGS 58
 5 QUERY: 60 RVTDLIHRESDEFPRQGTNFTLAEIGICEPS-PHRSGYCSDMGILHQGYSLSTGSDADSD 118
 SBJCT: 59 RVKDMVPQEAEEFCRTGTNFTLRELGLGEMTPPHGTLYRTDIGLPHCGYSMGASSDADLE 118
 10 QUERY: 119 TEGGMSPEHAIRLWGRGIKSRSSGLSSRENSALTTLT 155
 SBJCT: 119 ADTVLSPEHPVRLWGRSTRSGRSSCLSSRANSNLTLT 155

SCORE = 72.1 BITS (176), EXPECT = 8E-11
 IDENTITIES = 59/152 (38%), POSITIVES = 68/152 (43%), GAPS = 42/152 (27%)

15 QUERY: 285 PAPAPND--LATTP-----ESVQLQDSWVLNSNVPLETR----- 316
 SBJCT: 211 PSPAPTDHSLSGEPPAGSAQEPTHAQDNWLLNSNIPLETRNLGKQPFLGTLQDNLIEMDI 270
 20 QUERY: 317 -----HFLFKXXXXXXXXXXXXXXXXXVPLTSGTVYTPPPRLLPRNTFSRKAFK 363
 SBJCT: 271 LSASRHDGAYSDBGHFLFK-PGGTSPLFCTTSPGYPLTSSTVYSPPPRPLPRSTFSRPAFN 329
 25 QUERY: 364 LKKPSKYCSWKXXXXXXXXXXXXXXXXXXFYFI 395
 SBJCT: 330 LKKPSKYCNWKAALSAILISATLVILLAYFV 361

*FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

The 997-2733 amino acid fragment of the FCTR3bcde and f protein was also found to
 30 have 1695 of 1737 amino acid residues (97%) identical to, and 1695 of 1737 residues (97%)
 positive with the amino a 1737 amino acid residue protein KIAA1127 protein [*Homo sapiens*]
 (GenBank Acc:(AB032953) (SEQ ID NO:71), (Table 3S).

**Table 3S. BLASTP of FCTR3b, c, d, e, and f against *Homo sapiens* KIAA1127 protein
 (SEQ ID NO:71)**

35 >GI|6329763|DBJ|BAA86441.1| (AB032953) KIAA1127 PROTEIN [HOMO SAPIENS]
 LENGTH = 1737
 40 SCORE = 3295 BITS (8545), EXPECT = 0.0
 IDENTITIES = 1695/1737 (97%), POSITIVES = 1695/1737 (97%)
 45 QUERY: 997 TFFSAAPGQNPIVPETQVLHHEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLI 1056
 SBJCT: 1 TFFSAAPGQNPIVPETQVLHHEIELPGSNVKLRYLSSRTAGYKSLKITMTQSTVPLNLI 60
 50 QUERY: 1057 RVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 1116
 SBJCT: 61 RVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLSDAVSVGFYETCPSLI 120
 55 QUERY: 1117 LWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTTGENQFLTQQPAIITSIMGN 1176
 SBJCT: 121 LWEKRTALLQGFELDPSNLGGWSLDKHHILNVKSGILHKGTTGENQFLTQQPAIITSIMGN 180
 60 QUERY: 1177 GRRRSISCPCSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFPSRNVTSILELRNK 1236
 SBJCT: 181 GRRRSISCPCSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIRRIFFPSRNVTSILELRNK 240
 QUERY: 1237 EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 1296
 SBJCT: 241 EFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTKDLAGNSEVVAGTGEQCL 300
 QUERY: 1297 PFDEARCGDGGKAIDATILMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 1356

SBJCT: 301 |||||PFDEARCGDGGKAI DATLMSPRGIAVDKNGLMYFVDATMIRKVDQNGIISTLLGSNDLTA 360
 5 QUERY: 1357 VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQ 1416
 SBJCT: 361 VRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRITENHQVSI IAGRPMHCQ 420
 10 QUERY: 1417 VPGIDYSLSKXXXXXXXXXXXXXXXXX TGVL YITETDEKKINRLRQVTTNGEICLLAGAA 1476
 SBJCT: 421 VPGIDYSLSKLAIHSALESASAIASHTGVL YITETDEKKINRLRQVTTNGEICLLAGAA 480
 15 QUERY: 1477 SXXXXXXXXXXSYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 1536
 SBJCT: 481 SDCCKNDVNCNCYSGDDAYATDAILNSPSSLAVAPDGTIYIADLGNIRIRAVSKNKPVL 540
 20 QUERY: 1537 NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELDNNGNSLK 1596
 SBJCT: 541 NAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYSTDNDVTELDNNGNSLK 600
 25 QUERY: 1597 IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLGLMTYDGN TGGLATKSDET G 1656
 SBJCT: 601 IRRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLGLMTYDGN TGGLATKSDET G 660
 30 QUERY: 1657 WTTFYDYDHEGRLTNVTRPTGVVTS LHREMEKSITIDIENS NRDDVTITNLSSVEASY 1716
 SBJCT: 661 WTTFYDYDHEGRLTNVTRPTGVVTS LHREMEKSITIDIENS NRDDVTITNLSSVEASY 720
 35 QUERY: 1717 TVVQDQVRNSYQLCNGTLRVMYANGMISFHSEPHVLAGTITPTIGRCNISLPMENGLN 1776
 SBJCT: 721 TVVQDQVRNSYQLCNGTLRVMYANGMISFHSEPHVLAGTITPTIGRCNISLPMENGLN 780
 40 QUERY: 1777 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLR IYDQVG 1836
 SBJCT: 781 SIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKIYDDHRKFTLR IYDQVG 840
 45 QUERY: 1837 RPFLWL PSSGLAAVNVS YFFNGRLAGLQRGAMSER TDIDKQGRIVSRMFADGKVWSYSYL 1896
 SBJCT: 841 RPFLWL PSSGLAAVNVS YFFNGRLAGLQRGAMSER TDIDKQGRIVSRMFADGKVWSYSYL 900
 50 QUERY: 1897 DKSMVLLQLSQRQYIF EYDSSDRLLAVTMP SVARHSMSTHTSIGYIRNIYNPPESNASVI 1956
 SBJCT: 901 DKSMVLLQLSQRQYIF EYDSSDRLLAVTMP SVARHSMSTHTSIGYIRNIYNPPESNASVI 960
 55 QUERY: 1957 FDYSDDGRILKTSFLGTGRQV FYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 2016
 SBJCT: 961 FDYSDDGRILKTSFLGTGRQV FYKYGKLSKLSEIVYDSTAVTFGYDETTGVLKMNVLQSG 1020
 60 QUERY: 2017 GFSC TIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 2076
 SBJCT: 1021 GFSC TIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRIASIKPVISETPLPVDLY 1080
 65 QUERY: 2077 RYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 2136
 SBJCT: 1081 RYDEISGKVEHFGKFGVIYYDINQIITAVMTLSKHFDTHGRIKEVQYEMFRSLMYWMTV 1140
 QUERY: 2137 QYDSMGRVIKRELKLG PYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDXXXXXXXXXX 2196
 SBJCT: 1141 QYDSMGRVIKRELKLG PYANTTKYTYDYDGDGQLQSVAVNDRPTWRYSYDLNGLHLLNP 1200
 70 QUERY: 2197 XXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 2256
 SBJCT: 1201 GNSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEYNSKGLLTRAYNKASGWS 1260
 75 QUERY: 2257 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 2316
 SBJCT: 1261 VQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSNSEITSLYYDLQGHLFAM 1320
 80 QUERY: 2317 ESSSGEEYVVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVIGFHHGLYD 2376

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|||||
SBJCT: 1321 ESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYDSNPDFQMVGFGGLYD 1380

5  QUERY: 2377 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 2436
    |||||
SBJCT: 1381 PLTKLVHFTQRDYDVLAGRWTSPDYTMWKNVGKEPAPFNLYMFKSNNPLSSELDLKNYVT 1440

    |||||
10  QUERY: 2437 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 2496
    |||||
SBJCT: 1441 DVKSWLVMFGFQLSNIIPGFPRAKMYFVPPPYELSESQASENGQLITGVQQTTERHNQAF 1500

    |||||
15  QUERY: 2497 MALEGQVITKKLHASIREKAGHWFATTTPIIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 2556
    |||||
SBJCT: 1501 MALEGQVITKKLHASIREKAGHWFATTTPIIIGKGIMFAIKEGRVTTGVSSIASEDSRKVA 1560

    |||||
20  QUERY: 2557 SVLNNAYYLDKMHSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 2616
    |||||
SBJCT: 1561 SVLNNAYYLDKMHSIEGKDTHYFVKIGSADGDLVTLGTTIGRKVLESGVNVTVSQPTLL 1620

    |||||
25  QUERY: 2617 VNGRTRRFTNIEFQYSTLLLSIRYGLPTDLDDEKARVLDQARQALGTAWAKEQQKARD 2676
    |||||
SBJCT: 1621 VNGRTRRFTNIEFQYSTLLLSIRYGLPTDLDDEKARVLDQARQALGTAWAKEQQKARD 1680

    |||||
30  QUERY: 2677 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGKR 2733
    |||||
SBJCT: 1681 GREGSRLWTEGEKQQLLSTGRVQGYEGYYVLPVEQYPELADSSSNIQFLRQNMKGKR 1737

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The amino acid sequences of the FCTR3bcd and f proteins were also found to have 2528 of 2774 amino acid residues (91%) identical to, and 2557 of 2774 residues (92%) positive with, the 2765 amino acid residue protein neurestin alpha [*Rattus norvegicus*] (GenBank Acc:AF086607) (SEQ ID NO:72), shown in Table 3T.

Table 3T. BLASTP of FCTR3bcd and f against *Rattus norvegicus* Neurestin alpha (SEQ ID NO:72)

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35  >GI|9910320|REF|NP_064473.1| NEURESTIN ALPHA [RATTUS NORVEGICUS]
    GI|5712201|GB|AAD47383.1|AF086607_1 (AF086607) NEURESTIN ALPHA [RATTUS NORVEGICUS]
    LENGTH = 2765

    SCORE = 4988 BITS (12938), EXPECT = 0.0
    IDENTITIES = 2528/2774 (91%), POSITIVES = 2557/2774 (92%), GAPS = 50/2774 (1%)

40  QUERY: 1 MDVKDRRHRSILTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
    |||||
SBJCT: 1 MDVKDRRHRSILTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60

45  QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120
    |||+||||| || |||||
SBJCT: 61 VTDLVHRESDEFPSRQGANFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120

50  QUERY: 121 GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTITXXXXXXXXXXXXGRXXXXXXXXXXXX 180
    |||||
SBJCT: 121 GGMSPEHAIRLWGRGIKSRSSGLSSRENSALTITDSDNENKSDDDNGRPIPTSSSSLL 180

55  QUERY: 181 XXXXXXXXHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXX 240
    |||||
SBJCT: 181 PSAQLPSSHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240

60  QUERY: 241 NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPEVSQ 300
    |||||
SBJCT: 241 NHHSQSTLRPPLPPPHNHTLSHHSSANSNLNRSLTNRRSQIHAPAPAPNDLATTPEVSQ 300

    |||||
QUERY: 301 LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXYPPLTSGTVYTPPPRLLPRNTFSRK 360

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10000198 1000860

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      |||
SBJCT: 301 LQDSWVLNSNVPLETRHFLFKTSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360

      |||
QUERY: 361 AFKLLKPSKYCSWKXXXXXXXXXXXXXXXXXXFYI----- 395
5      |||
SBJCT: 361 AFKLLKPSKYCSWKCAALSAIAAALLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420

      |||
QUERY: 396 -----VPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLK 439
10      |||
SBJCT: 421 GLPGNDDVATVPSSGGKVPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLK 480

      |||
QUERY: 440 FNISLGKDALFGVYIRRGLPSSHAQYDFMERLDGKEKWSVVEsprerrSIQTLVQNEAVF 499
15      |||
SBJCT: 481 FNISLGKDALFGVYIRRGLPSSHAQYDFMERLDGKEKWSVVEsprerrSIQTLVQNEAVF 540

      |||
QUERY: 500 VQYLDVGLWHLAFYNDGDKEMVSFNTVVLDVQDCPRNCHGNGECVSGVCHCFPGFLGA 559
      |||
SBJCT: 541 VQYLDVGLWHLAFYNDGDKEMVSFNTVVLDVQDCPRNCHGNGECVSGVCHCFPGFLGA 600

      |||
QUERY: 560 DCAKAACPVLCSGNGQYSGKTCQCYSGWKGAECDVPMNQCIDPSCGGHGS CIDGNCVCSA 619
20      |||
SBJCT: 601 DCAKAACPVLCSGNGQYSGKTCQCYSGWKGAECDVPMNQCIDPSCGGHGS CIDGNCVCAA 660

      |||
QUERY: 620 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYPDT 679
25      |||
SBJCT: 661 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYPDS 720

      |||
QUERY: 680 GLCSCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEGWTGAACDQRVCHPRCIEHGTC 739
      |||
30      |||
SBJCT: 721 GLCNCDPNWMGPDCSVEVCSVDCGTHGVCIGGACRCEGWTGAACDQRVCHPRCIEHGTC 780
      |||
      *****
QUERY: 740 KDGKCECREGWNGEHTIGRQTAGTETDGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 799
      |||
35      |||
SBJCT: 781 KDGKCECREGWNGEHTI-----DGCPLCNGNGRCTLGQNSWQCVCQTGWRGPGC 831

      |||
QUERY: 800 NVAMETSCADNKDNEGDGLVDCLDPDCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 859
      |||
SBJCT: 832 NVAMETSCADNKDNEGDGLVDCLDPDCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 891

      |||
40      |||
QUERY: 860 SFYDRIKLLAGKDSITHIIPGENPFNSSLVSLIRGQVVTDTGTPLVGVNVSFVKYPKYGYT 919
      |||
SBJCT: 892 SFYDRIKLLAGKDSITHIIPGDNPFNSSLVSLIRGQVVTDTGTPLVGVNVSFVKYPKYGYT 951

      |||
45      |||
QUERY: 920 ITRQDGTFDLIANGGASLT LHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 979
      |||
SBJCT: 952 ITRQDGTFDLIANGGASLT LHFERAPFMSRERTVWLPWNSFYAMDTLVMKTEENSIPSCD 1011

      |||
QUERY: 980 LSGFVRPDPIIISSPLSTFFSAAQPNIIVPETQVLHEEIELPGSNVKLRYLSSRTAGYK 1039
      |||
50      |||
SBJCT: 1012 LSGFVRPDPIIISSPLSTFFSASPAANPIIVPETQVLHEEIELPGTNVKLRYLSSRTAGYK 1071

      |||
QUERY: 1040 SLLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099
      |||
55      |||
SBJCT: 1072 SLLKITMTQSTVPLNLRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1131

      |||
QUERY: 1100 DAVSVGFYETCPSLILWEKRTALLQGFE LDP SNLGGWSLDKHHTLNKSGILHKTGE 1159
      |||
SBJCT: 1132 DAVSVGFYETCPSLILWEKRTALLQGFE LDP SNLGGWSLDKHHTLNKSGILLKTGE 1191

      |||
60      |||
QUERY: 1160 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219
      |||
SBJCT: 1192 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1251

      |||
65      |||
QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
      |||
SBJCT: 1252 RIFPSRNVTSILELRNKEFKHSNPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1311

      |||
QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
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|||||+|||||
SBJCT: 1312 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAVDATLMSPRGIAVDKNGLMYFVDATMIRKV 1371

5
QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
|||||
SBJCT: 1372 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1431

10
QUERY: 1400 TENHQVSIIAGRPMHCQVPGIDYSLSKXXXXXXXXXXXXXXXXXGVLITETDEKKINR 1459
|||||
SBJCT: 1432 TENHQVSIIAGRPMHCQVPGIDYSLSKLAIHSALESASAIASHTGVLYITETDEKKINR 1491

15
QUERY: 1460 LRQVTNNGEICLLAGAASXXXXXXXXXXSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
|||||
SBJCT: 1492 LRQVTNNGEICLLAGAASDCCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1551

20
QUERY: 1520 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1579
|||||
SBJCT: 1552 DLGNIRIRAVSKNKPVLNAFNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1611

25
QUERY: 1580 TDNDVTEIDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVGTNGGLKVVSTQNLELGLM 1639
|||||
SBJCT: 1612 ADNDVTEIDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVGTNGGLKAVSTQNLELGLM 1671

30
QUERY: 1640 TYDGNTEGLLATKSDEGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
|||||+|||||
SBJCT: 1672 TYDGNTEGLLATKSDEGTWTFYDYDHEGRLTNVTRPTGVVTSLHREMEKSITVDIENSNR 1731

35
QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
|+|||||+|||||+|
SBJCT: 1732 DNDVTVITNLSSVEASYTVVQDQVRNSYQLCSNGTLRVMYANGMGVFSFHSEPHVLAGTIT 1791

40
QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
|||||
SBJCT: 1792 PTIGRCNISLPMENGLNSIEWRLRKEQIKGKVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1851

45
QUERY: 1820 YDDHRKFTLRRIIDYQVGRPLWLPSGLAAVNVSFFNGRLAGLQRGAMSSERTDIDKQGR 1879
|||||
SBJCT: 1852 YDDHRKFTLRRIIDYQVGRPLWLPSGLAAVNVSFFNGRLAGLQRGAMSSERTDIDKQGR 1911

50
QUERY: 1880 IVSRMFADGKVSYSYLDKSMVLLQLSQRYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1939
|||||
SBJCT: 1912 IVSRMFADGKVSYSYLDKSMVLLQLSQRYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1971

55
QUERY: 1940 GYIRNIYNPPESNASVIFDYSDDGRLKTSFSLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
|||||
SBJCT: 1972 GYIRNIYNPPESNASVIFDYSDDGRLKTSFSLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2031

60
QUERY: 2000 GYDETTGVLKMNVLQSGGFCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059
|||||+|||||+|
SBJCT: 2032 GYDETTGVLKMNVLQSGGFCTIRYRKIGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2091

65
QUERY: 2060 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2119
|||||
SBJCT: 2092 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2151

QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPANTTKYTYDYDGDGQLQSVAVNDRP 2179
|||||
SBJCT: 2152 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPANTTKYTYDYDGDGQLQSVAVNDRP 2211

QUERY: 2180 TWRYSDXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
|||||
SBJCT: 2212 TWRYSDLNGNLHLLNPGNSARLMPRLYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2271

QUERY: 2240 NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
|||||+|||||
SBJCT: 2272 NSKGLLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2331

QUERY: 2300 SEITSLYIDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359

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SBJCT: 2332 SEITSLYYDLQGHLFAMESSSGEEYYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2391
5  QUERY: 2360 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLGRWTSPTYTMWKNVVGKEPAPFNLYMF 2419
    |||||||+|||||
SBJCT: 2392 SNPDFQMVIGFHGGLYDPLTKLVHFTQRDYDVLGRWTSPTYTMWRNVVGKEPAPFNLYMF 2451
10  QUERY: 2420 KSNPNLSSELDLKNYVTDVKSWMVFGFQLSNII PGFPRAKMYFVPPPYELSESQASENG 2479
    |+|||+|||+|||||
SBJCT: 2452 KNNNPLSNELDLKNYVTDVKSWMVFGFQLSNII PGFPRAKMYFVPPPYELSESQASENG 2511
15  QUERY: 2480 QLITGVQQTTERHNOAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
    |||||||+|||||+|||||
SBJCT: 2512 QLITGVQQTTERHNOAFMALEGQVISKKLHAGIREKAGHWFATTTPIIGKGIMFAIKEGR 2571
20  QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGR 2599
    |||||||+|||||
SBJCT: 2572 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGAADGDLVTLGTTIGR 2631
25  QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
    |||||||
SBJCT: 2632 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2691
30  QUERY: 2660 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2719
    |||||||
SBJCT: 2692 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2751
    QUERY: 2720 SNIQFLRQNMKGKR 2733
    |||||||
    SBJCT: 2752 SNIQFLRQNMKGKR 2765

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* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

The amino acid sequences of the FCTR3bcde and f proteins were also found to have 2536 of 2774 amino acid residues (91%) identical to, and 2558 of 2774 residues (91%) positive with, the 2764 amino acid residue protein Odd Oz/ten-m homolog 2 (*Drosophila*) (GenBank Acc:NP_035986.2) (SEQ ID NO:65), shown in Table 3U.

Table 3U. BLASTP of FCTR3bcde and f against Odd Oz/ten-m homolog 2 (SEQ ID NO:65)

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40  >GI|7657415|REF|NP_035986.2| ODD OZ/TEN-M HOMOLOG 2 (DROSOPHILA); ODD OZ/TEN-M
    HOMOLOG 3
        (DROSOPHILA) [MUS MUSCULUS]
    GI|4760778|DBJ|BAA77397.1| (AB025411) TEN-M2 [MUS MUSCULUS]
    LENGTH = 2764
45  SCORE = 4996 BITS (12961), EXPECT = 0.0
    IDENTITIES = 2536/2774 (91%), POSITIVES = 2558/2774 (91%), GAPS = 51/2774 (1%)
50  QUERY: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
    |||||||
    SBJCT: 1 MDVKDRRHRSLTRGRCGKECRYTSSSLDSEDCRVPTQKSYSSSETLKAYDHDSRMHYGNR 60
55  QUERY: 61 VTDLIHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120
    |||+|||
    SBJCT: 61 VTDLVHRESDEFPRQGTNFTLAELGICEPSPHRSGYCSMDGILHQGYSLSTGSDADSDTE 120
60  QUERY: 121 GGMSPEHAIRLWGRGIKSRSSSGLSSRENSALTLTXXXXXXXXXXXXXGRXXXXXXXXXXXXX 180
    |||||||
    SBJCT: 121 GGMSPEHAIRLWGRGIKSRSSSGLSSRENSALTLTDSNENKSDDDNGRPIPTSSSSLL 180

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QUERY: 181 XXXXXXXXHNPPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACXXXXXXXXXXXX 240
 SBJCT: 181 PSAQLPSSHNPVSCQMPLLDSNTSHQIMDTNPDEEFSPNSYLLRACSGPQQASSSGPP 240
 5 QUERY: 241 NHHSQXXXXXXXXXXXXXXXXXXXXXXXXXXXXXQIHAPAPAPNDLATTPEVQ 300
 SBJCT: 241 NHHSQSTLRPLPPPHNHTLSHHSSANSINRNSLTNRRSQIHAPAPAPNDLATTPEVQ 300
 10 QUERY: 301 LQDSWVLNSNVPLETRHFLFKXXXXXXXXXXXXXXXXXYPLTSGTVYTPPPRLLPRNTFSRK 360
 SBJCT: 301 LQDSWVLNSNVPLETRHFLFKTSSSGSTPLFSSSSPGYPLTSGTVYTPPPRLLPRNTFSRK 360
 QUERY: 361 AFKLLKPSKYCSWKXXXXXXXXXXXXXXXXXXFYI----- 395
 15 SBJCT: 361 AFKLLKPSKYCSWKCAALSAIAAALLAILLAYFIAMHLLGLNWQLQPADGHTFNNGVRT 420
 QUERY: 396 -----VPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLK 439
 20 SBJCT: 421 GLPGNDVATVPSSGKVPWSLKNSSIDSGEAEVGRRTQEVPPGVFWRSQIHISQPQFLK 480
 QUERY: 440 FNISLGKDALFGVYIRRLPPSHAQYDFMERLDGKEKWSVVEsprerrsiQTLVQNEAVF 499
 SBJCT: 481 FNISLGKDALFGVYIRRLPPSHAQYDFMERLDGKEKWSVVEsprerrsiQTLVQNEAVF 540
 25 QUERY: 500 VQYLDVGLWHLAFYNDGKDKEVMSFNTVVLDVQDCPRNCHGNCEVSGVCHCFPGFLGA 559
 SBJCT: 541 VQYLDVGLWHLAFYNDGKDKEVMSFNTVVLDVQDCPRNCHGNCEVSGVCHCFPGFLGA 600
 30 QUERY: 560 DCAKAACPVLCSGNGQYSGKTCQCYSGWKGAECVPMNQCIDPSCGGHGSIDGNCVCSA 619
 SBJCT: 601 DCAKAACPVLCSGNGQYSGKTCQCYSGWKGAECVPMNQCIDPSCGGHGSIDGNCVCAA 660
 QUERY: 620 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYPDT 679
 35 SBJCT: 661 GYKGEHCEEVDCLDPTCSSHGVCVNGECLCSPGWGGLNCELARVQCPDQCSGHGTYPDS 720
 QUERY: 680 GLCSCDPNWMGPDSCSVEVCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 739
 40 SBJCT: 721 GLCSCDPNWMGPDSCSV-VCSVDCGTHGVCIGGACRCEEGWTGAACDQRVCHPRCIEHGTC 779

 QUERY: 740 KDKGCECREGWNGEHCTIGRTAGTETDGCPLCNGNGRCTLGQNSWQVCQTGWGRPGC 799
 SBJCT: 780 KDKGCECREGWNGEHCTI-----DGCPLCNGNGRCTLGQNSWQVCQTGWGRPGC 830
 45 QUERY: 800 NVAMETSCADNKDNEGDGLVDCCLDPCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 859
 SBJCT: 831 NVAMETSCADNKDNEGDGLVDCCLDPCCLQSACQNSLLCRGSRDPLDIIQQGQTDWPAVK 890
 50 QUERY: 860 SFYDRIKLLAGKDSITHIPGENPFNSSLSLIRGQVVTMDGTPLVGVNVSFVKYPKYGYT 919
 SBJCT: 891 SFYDRIKLLAGKDSITHIPGDNPFNSSLSLIRGQVVTMDGTPLVGVNVSFVKYPKYGYT 950
 QUERY: 920 ITRQDGTFDLIANGGASLTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 979
 55 SBJCT: 951 ITRQDGTFDLIANGGSALTTLHFERAPFMSQERTVWLPWNSFYAMDTLVMKTEENSIPSCD 1010
 QUERY: 980 LSGFVRPDPPIIISSPLSTFFSAAPQNPVIVPETQVLHHEIELPGSNVKLRYLSSRTAGYK 1039
 60 SBJCT: 1011 LSGFVRPDPPIIISSPLSTFFSASPASNPVIVPETQVLHHEIELPGTNVKLRYLSSRTAGYK 1070
 QUERY: 1040 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLASTFIWDKTDAYGQRVYGLS 1099
 SBJCT: 1071 SLLKITMTQSTVPLNLIRVHLMVAVEGHLFQKSFQASPNLAYTFIWDKTDAYGQRVYGLS 1130
 65 QUERY: 1100 DAVSVGFYEYETCPSLILWEKRTALLQGFELDPNSLGGWSLDKHHTLNKSGILHKGTE 1159
 SBJCT: 1131 DAVSVGFYEYETCPSLILWEKRTALLQGFELDPNSLGGWSLDKHHTLNKSGILHKGTE 1190

QUERY: 1160 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLYVGDFNYIR 1219
 ||||||||||||||||||||||||||||||||||||||||||||+|||||||
 SBJCT: 1191 NQFLTQQPAIITSIMGNRRRSISCPSCNGLAEGNKLLAPVALAVGIDGSLFVGDFNYIR 1250
 5 QUERY: 1220 RIFPSRNVTSILELRNKEFKHSNNPAHKYYLAVDPVSGSLYVSDTNSRRIYRVKSLSGTK 1279
 ||||||||||||||||||||||||+|||||||+|||||||
 SBJCT: 1251 RIFPSRNVTSILELRNKEFKHSNSPGHKYYLAVDPVTGSLYVSDTNSRRIYRVKSLSGAK 1310
 10 QUERY: 1280 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1339
 ||||||||||||||||||||||||+|||||||
 SBJCT: 1311 DLAGNSEVVAGTGEQCLPFDEARCGDGGKAIDATLMSPRGIAVDKNGLMYFVDATMIRKV 1370
 QUERY: 1340 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1399
 ||||||||||||||||||||||||||||||||||||||||||||
 15 SBJCT: 1371 DQNGIISTLLGSNDLTAVRPLSCDSSMDVAQVRLEWPTDLAVNPMDNSLYVLENNVILRI 1430
 QUERY: 1400 TENHQVSIAGRPMHCQVPGIDYSLKXXXXXXXXXXXXXXXXXXTGVLYITETDEKKINR 1459
 ||||||||||||||||||||||||| ||||||||||||||||
 20 SBJCT: 1431 TENHQVSIAGRPMHCQVPGIDYSLKLAHSALESASAIAISHTGVLYITETDEKKINR 1490
 QUERY: 1460 LRQVTTNGEICLLAGAASXXXXXXXXXXSGDDAYATDAILNSPSSLAVAPDGTIYIA 1519
 ||||||||||||||||| |||||||||||||||||
 SBJCT: 1491 LRQVTTNGEICLLAGAASDCDCKNDVNCICYSGDDAYATDAILNSPSSLAVAPDGTIYIA 1550
 25 QUERY: 1520 DLGNIRIRAVSKNKPVLNAPNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1579
 |||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1551 DLGNIRIRAVSKNKPVLNAPNQYEAASPGEQELYVFNADGIHQYTVSLVTGEYLYNFTYS 1610
 30 QUERY: 1580 TDNDVTELDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVGTINGGLKVVSTQNLLEGLM 1639
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 1611 ADNDVTELDNNGNSLKIIRDSSGMPRHLLMPDNQIITLTVGTINGGLKAVSTQNLLEGLM 1670
 QUERY: 1640 TYDGNTGLLATKSDETGWTTFYDHDHGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1699
 |||||||||||||||||||||||||||||||||||||
 35 SBJCT: 1671 TYDGNTGLLATKSDETGWTTFYDHDHGRLTNVTRPTGVVTSLHREMEKSITIDIENSNR 1730
 QUERY: 1700 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMGISFHSEPHVLAGTIT 1759
 ||||||||||||||||||||||||||||||||||||| + |||||||||
 40 SBJCT: 1731 DDDVTVITNLSSVEASYTVVQDQVRNSYQLCNGTLRVMYANGMAVSFHSEPHVLAGTIT 1790
 QUERY: 1760 PTIGRCNISLPMENGLNSIEWRLRKEQIKGVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1819
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 1791 PTIGRCNISLPMENGLNSIEWRLRKEQIKGVTIFGRKLRVHGRNLLSIDYDRNIRTEKI 1850
 45 QUERY: 1820 YDDHRKFTLRRIIDYQVGRPFLWLPSSGLAAVNVSFFNGRLAGLQRGAMSERTDIDKQGR 1879
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 1851 YDDHRKFTLRRIIDYQVGRPFLWLPSSGLAAVNVSFFNGRLAGLQRGAMSERTDIDKQGR 1910
 50 QUERY: 1880 IVSRMFADGKVWSYSYLDKSMVLLQLSQROYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1939
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 1911 IVSRMFADGKVWSYSYLDKSMVLLQLSQROYIFEYDSSDRLLAVTMPVARHSMSTHTSI 1970
 QUERY: 1940 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 1999
 |||||||||||||||||||||||||||||||||||||
 55 SBJCT: 1971 GYIRNIYNPPESNASVIFDYSDGRILKTSFLGTGRQVFYKYGKLSKLSEIVYDSTAVTF 2030
 QUERY: 2000 GYDETTGVLKMNVLQSGGFCTIRYRKIGPLVDKQIYRFSEEGMVNARFDYTYHDNSFRI 2059
 ||||||||||||||||||||||||+|||||||+|||||||
 60 SBJCT: 2031 GYDETTGVLKMNVLQSGGFCTIRYRKVGPLVDKQIYRFSEEGMINARFDYTYHDNSFRI 2090
 QUERY: 2060 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2119
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 2091 ASIKPVISETPLPVDLYRYDEISGKVEHFGKFGVIYYDINQIITTAVMTLSKHFDTHGRI 2150
 65 QUERY: 2120 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPYANTTKYTYDYDGDGQLQSVAVNDRP 2179
 |||||||||||||||||||||||||||||||||||||
 SBJCT: 2151 KEVQYEMFRSLMYWMTVQYDSMGRVIKRELKLGYPYANTTKYTYDYDGDGQLQSVAVNDRP 2210

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QUERY: 2180 TWRYSYDXXXXXXXXXXSVRLMPLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2239
      |||||      | |||||
SBJCT: 2211 TWRYSYDLNGLHLLNPGNSARLMLRYDLRDRITRLGDVQYKIDDDGYLCQRGSDIFEY 2270

5  QUERY: 2240 NSKGILLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2299
      |||||
SBJCT: 2271 NSKGILLTRAYNKASGWSVQYRYDGVGRRASYKTNLGHHLQYFYSDLHNPTRITHVYNHSN 2330

10 QUERY: 2300 SEITSLYYDLQGHLFAMESSSGEEYVASDNTGTPLAVFSINGLMIKQLQYTAYGEIYYD 2359
      |||||+|||
SBJCT: 2331 SEITSLYYDLQGHLFAMESSSGEEYVASDNTGTPLAVYSINGLMIKQLQYTAYGEIYYD 2390

      QUERY: 2360 SNPDFQMVGIFHGGLYDPLTKLVHFTQRDYDVLGRWTS PDYTMWKNVGKEPAPFNLYMF 2419
      |||||+|||
15 SBJCT: 2391 SNPDFQMVGIFHGGLYDPLTKLVHFTQRDYDVLGRWTS PDYTMWRNVGKEPAPFNLYMF 2450

      QUERY: 2420 KSNPNLSSELDLKNYVTDVKSWMFQFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2479
      |+|||+|||
20 SBJCT: 2451 KNNPNLSNELDLKNYVTDVKSWMFQFQLSNIIPGFPRAKMYFVPPPYELSESQASENG 2510

      QUERY: 2480 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2539
      |||||+|||
SBJCT: 2511 QLITGVQQTTERHNQAFMALEGQVITKKLHASIREKAGHWFATTTPIIGKGIMFAIKEGR 2570

25 QUERY: 2540 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGSADGDLVTLGTTIGR 2599
      |||||+|||
SBJCT: 2571 VTTGVSSIASEDSRKVASVLNNAYYLDKMHYSIEGKDTHYFVKIGAADGDLVTLGTTIGR 2630

      QUERY: 2600 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAR 2659
      |||||
30 SBJCT: 2631 KVLESGVNVTVSQPTLLVNGRTRRFTNIEFQYSTLLLSIRYGLTPDTLDEEKARVLDQAG 2690

      QUERY: 2660 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2719
      |||||
35 SBJCT: 2691 QRALGTAWAKEQQKARDGREGSRLWTEGEKQQLSTGRVQGYEGYYVLPVEQYPELADSS 2750

      QUERY: 2720 SNIQFLRQNE MGKR 2733
      |||||
40 SBJCT: 2751 SNIQFLRQNE MGKR 2764

* = FCTR3F DOES NOT CONTAIN THESE AMINO ACIDS

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FCTR3 is related to rat neurestin, a gene implicated in neuronal development (Otaki JM, Firestein S Dev Biol 1999 Aug 1;212(1):165-81) Neurestin shows homology to human gamma-heregulin, a Drosophila receptor-type pair-rule gene product, Odd Oz (Odz) / Ten(m), and Ten(a). Neurestin has putative roles in synapse formation and brain morphogenesis. A mouse neurestin homolog, DOC4, has independently been isolated from the NIH-3T3 fibroblasts. DOC4 is also known as tenascin M (TNM), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The significant homology to these molecules and in particular, γ -heregulin, have important implications regarding the potential contribution of FCTR3 to disease progression. Heregulin is the ligand for HER-2/ErbB2/NEU, a proto-oncogene receptor tyrosine kinase implicated in breast and prostate cancer progression that was originally identified in rat neuro/glioblastoma cell lines. Extopic expression of HER-2/ErbB2/NEU in MDA-MB-435 breast adenocarcinoma cells confers chemoresistance to Taxol-induced apoptosis relative to vector transfected control cells (Yu et

al. Overexpression of ErbB2 blocks Taxol-induced apoptosis by up-regulation of p21Cip1, which inhibits p34Cdc2 kinase. Molec. Cell 2: 581-591, 1998).

FCTR3 related tenascins and cancer biology

As mentioned, FCTR3 also has significant homology to DOC4, (AKA tenascin M), a *Drosophila* pair-rule gene homolog containing extracellular EGF-like repeats. The tenascins are a growing family of extracellular matrix proteins that play prominent roles in tissue interactions critical to embryogenesis. Overexpression of tenascins has been described in multiple human solid malignancies.

The role of the tenascin family of related proteins is to regulate epithelial-stromal interactions, participate in fibronectin-dependent cell attachment and interaction. Indeed, tenascin-C (TN) is overexpressed in the stroma of malignant ovarian tumours particularly at the interface between epithelia and stroma leading to suggestions that it may be involved in the process of invasion (Wilson et al (1996) Br J Cancer 74: 999-1004). Tenascin-C is considered a therapeutic target for certain malignant brain tumors (Gladson CL : J Neuropathol Exp Neurol 1999 Oct;58(10):1029-40). Stromal or moderate to strong periductal Tenascin-C expression in DCIS (ductal carcinoma in situ) correlates with tumor cell invasion. (Jahkola et al. Eur J Cancer 1998 Oct;34(11):1687-92. Tenascin-C expression at the invasion border of early breast cancer is a useful predictor of local and distant recurrence. Jahkola T, et al. Br J Cancer. 1998 Dec;78(11):1507-13). Tenascin (TN) is an extracellular matrix protein found in areas of cell migration during development and expressed at high levels in migratory glioma cells. Treasurywala S, Berens ME Glia 1998 Oct;24(2):236-43 Migration arrest in glioma cells is dependent on the alphaV integrin subunit. Phillips GR, Krushel LA, Crossin KL J Cell Sci 1998 Apr;111 (Pt 8):1095-104 Domains of tenascin involved in glioma migration. Finally, tenascin expression in hormone-dependent tissues of breast and endometrium indicate that Tenascin expression reflects malignant progression and is down-regulated by antiprogesterins during terminal differentiation of rat mammary tumors (Vollmer et al. Cancer Res 1992 Sep 1;52(17):4642-8)

Potential role of FCTR3 in oncologic disease progression:

Based on the bioactivity described in the medical literature for related molecules, FCTR3 may play a role in one or more aspects of tumor cell biology that alter the interactions of tumor epithelial cells with stromal components. In consideration, FCTR3 may play a role in the following malignant properties:

Autocrine/paracrine stimulation of tumor cell proliferation

Autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy

Local tissue remodeling, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis.

- 5 Tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance.

Therapeutic intervention targeting FCTR3 in oncologic and central nervous system indications:

- 10 Predicted disease indications from expression profiling in 41 normal human tissues and 55 human cancer cell lines (see Example 2) include a subset of human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas. Targeting of FCTR3 by human or humanized monoclonal antibodies designed to disrupt predicted interactions of FCTR3 with its cognate ligand may
- 15 result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Identification of small molecules that specifically/selectively interfere with downstream signaling components engaged by FCTR3/ligandinteractions would also be expected to result in significant anti-tumor/anti-metastatic activity and the amelioration of associated symptomatology. Likewise, modified antisense ribonucleotides or antisense gene
- 20 expression constructs (plasmids, adenovirus, adeno-associated viruses, "naked" DNA approaches) designed to diminish the expression of FCTR3 transcripts/messenger RNA (mRNA) would be anticipated based on predicted properties of FCTR3 to have anti-tumor impact.

- Based on the relatedness to neurestin and heregulins, as well as its high level
- 25 expression in brain tissue, FCTR3 may also be used for remyelination in order to promote regeneration/repair/remyleination of injured central nervous system cells resulting from ischemia, brain trauma and various neurodegenerative diseases.. This postulate is based on reports indicating that neuregulin, glial growth factor 2, diminishes autoimmune demyelination and enhances remyelination in a chronic relapsing model for multiple sclerosis
- 30 (Cannella et al. . Proc. Nat. Acad. Sci. 95: 10100-10105, 1998). The expression of the related molecule neurestin can be induced in external tufted cells during regeneration of olfactory sensory neurons.

FCTR4

FCTR4 is a plasma membrane protein related to NF-Kappa-B P65delta3 protein. The clone is expressed in fetal liver tissues.

The novel FCTR4 nucleic acid of 609 nucleotides (also referred to as 29692275.0.1) is shown in Table 4A. An ORF begins with an ATG initiation codon at nucleotides 99-101 and ends with a TAA codon at nucleotides 522-524. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 4A, and the start and stop codons are in bold letters.

Table 4A. FCTR4 Nucleotide Sequence (SEQ ID NO:14)

CTGACATACTATATTAGTTGTTTGTTCACCTGTCTCCACTCCAGCTAGAAATATAAGTTCCATAGGGCAGAGTTTTTGTTCAC
CTGCTATATTTTATAAGCATGAATGAATGCATGAACGAATGGACTGATAACCCACAAGCCAAAGACCTCCATGACCTGCC
ACTGCCCTCCTTTTATTTTATTCTCACCTCTACCAATACTAAATCACCTAGTTATGTAAATACGATATGCACCTTTCATGG
CCCCTTGCTTTTGTATATGCTGTCCCTTTGCCTGGAATATAAACTCTCAAAATACCATCCACATTTTAAATCTTCTCC
AGAAAGCTTCCTCTGTCCACCCCACTCCACCCCATATAGAGTAAGTCAGTCTTTCTTTGTGCTACATTGTACC
TGTATCTACAGTGGCTCTAATCAAAGTGCCTGTGTCTCTCACTTCCCTAGATTGTGAACCTTTTGAGGCTGAAGACTACT
TATTCATCTCTTTACCTCAATGCCTAGGACAGGACCTTCATAAAGCACTACTCTATAAATGTTGAAACATATGCATGA
CTATTCTGTAACAGGAATGAAAATATGGCATTTCAGAAGTCACTACTC

The FCTR4 protein encoded by SEQ ID NO:14 has 141 amino acid residues and is presented using the one-letter code in Table 4B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the plasma membrane with a certainty of 0.6000. The most likely cleavage site for a peptide is between amino acids 39 and 40, *i.e.*, at the dash in the amino acid sequence ACT-CCA, based on the SignalP result. The predicted molecular weight of this protein is 16051.5 Daltons.

Table 4B. Encoded FCTR4 protein sequence (SEQ ID NO:15).

MNECMNEWTDNPQAKDLHDLPLPSFHFILSTNTKSPSYVNTICTFMAPCFVICCSLCLEYKLSKYHPHFKIFSRKLPLSTPT
LPFPYRVSQSFLCATFVPVSTVALIKLHCVSHFLDCELFEAEDYLFISLPPMPRTGPS

The predicted amino acid sequence was searched in the publicly available GenBank database FCTR4 protein showed 30 % identities (22 over 72 amino acids) and 43% homologies (31 over 72 amino acids) with hypothetical 10 kD protein of *Trypanosoma cruzi* (86 aa; ACC:Q99233) shown in Table 4C. The best homologies with a human protein were 54 % identities (114 over 343 amino acids) with NF-Kappa-B P65delta3 protein (71 aa fragment; ACC:Q13313) (SEQ ID NO:77).

Table 4C. BLASTP of FCTR4 against protein sequences

BLAST X search results are shown below:

ptnr:SPTREMBL-ACC:Q99233 HYPOTHETICAL 10 KD PROTEIN +3, 68, 0.60, 1, (SEQ ID NO:73)

ptnr:SPTREMBL-ACC:Q16896 GABA RECEPTOR SUBUNIT - AEDES +3, 66, 0.81, 4
(SEQ ID NO:74)

ptnr:SPTREMBL-ACC:O76473 GABA RECEPTOR SUBUNIT - LEPTI... +3, 66, 0.99, 2
(SEQ ID NO:75)

5 ptnr:TREMBLNEW-ACC:AAD28317 F13J11.13 PROTEIN - Arabid... +3, 62, 0.99, 1 (SEQ
ID NO:76)

Based upon homology, FCTR4 proteins and each homologous protein or peptide may
share at least some activity.

10

FCTR5

FCTR5 is a protein bearing sequence homology to human complement C1R
component precursor. The clone is expressed in breast, heart, lung, fetal lung, salivary gland,
adrenal gland, spleen, kidney, and fetal kidney.

15

The novel FCTR5 nucleic acid of 1667 nucleotides (also referred to as
32125243.0.21) is shown in Table 5A. An ORF begins with an ATG initiation codon at
nucleotides 34-36 and ends with a TGA codon at nucleotides 1495-1497. A putative
untranslated region upstream from the initiation codon and downstream from the termination
codon is underlined in Table 5A, and the start and stop codons are in bold letters.

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Table 5A. FCTR5a Nucleotide Sequence (SEQ ID NO:16)

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GTTCTCTCGCAGGTCCCAGATGTCCAGTTCAGATG**CCT**TGGACCCAGAGTGTGGGGAAATATCTCTGGAGAAGCCCTCA
CTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCTCCAGGCTTGCCCAACCCGGGCTCCGTCC
TCTTGGCCCAAGAGCTACCCAGCAGCTGACATCCCCCGGTACCCAGAGCCGTATGGCAAAGGCCAAGAGAGCAGCACG
GACATCAAGGCTCCAGAGGGCTTTGCTGTGAGGCTCGTCTTCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTGCAGG
GGACTCTGTGCACAACTCTCATTCGTTCGGTTCGGATCCAAGCCAGTTCGTGTGGTCAGCAAGGCTCCCTCTGGGCAGGCCCC
CTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTTTGGCGCTGACCTTCGACACACAGCCTTCCTCGGAGAACAAGACT
GCCCACTCCACAAGGGCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAAGTATAGTCAGCCCATCAGCGAGGCCAGCAG
GGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCCTGCCAAGGTCCAGAACCACTGCCAGGAGCCCTATTATCAGGCCG
CGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGACCTGGAAGACAGACAGGATGGGAGGAGGTTCTTCAGTGTATG
CCTGTCTGCGGACGGCCAGTCAACCCATTGCCAGAAATCAGACGACCCCTCGGTTCTTCAGAGCCAAGCTGGGCAACTT
CCCTGGCAAGCCTTCACAGTATCCACGGCCGTGGGGGCGGGCCCTGCTGGGGGACAGATGGATCCTCACTGCTGCCC
ACACATCTACCCCAAGGACAGTGTTCCTCTCAGGAAGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGAT
GAGATGCTGAAACTGGGGAACCAACCTGTCCACCGTGTCTGTGACCCCGACTACCGTCAGAATGAGTCCCATAACTT
TAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAACGTCCTCCCGGTCTGTCTGCCCGATA
ATGAGACCCCTCTACCGCAGCGGCTTGTGGGGTACGTCACTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTG
AAGTACTCGAGGCTGCCTGTAGCTCCCAGGGAGGCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGTTTTC
TGACAATATGTTCTGTGTTGGGGATGAGACGCAAGGCCAGTGTCTGCCAGGGGGACAGTGGCAGCCTCTATGTGGTAT
GGGACAATCATGCCCATCACTGGGTGGCCACGGGCATTGTGCTCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTAC
ACCAAGGTGCTCAGCTATGTGGACTGGATCAAGGGAGTGTGAATGGCAAGAATT**GACCCTGGGGGCTTGAACAGGGACT**
GACCAGCACAGTGGAGGCCCAAGCAGAGGGCCTGGAGTGAAGTGAACACTGGGGTAGGGGTGGGGGTTTCTCT
TGCAGTGGCTTGGTGAACAGTGTATGTGAATAGGATTTCCCTTTTTTTTTTTTTTAAAAA

The FCTR5 protein encoded by SEQ ID NO:16 has 487 amino acid residues, and is presented using the one-letter code in Table 5B. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5 protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5B. Encoded FCTR5a protein sequence (SEQ ID NO:17).

MPGPRVWGKYLWRSPHSKGCPCGAMWWLLWGVQLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF
QDFDLEPSQDCAGDSVTISFVGSQDPSQFCGQGSPLGRPPGQREFVSSGRSLRLTFRTPQSSSENKTAHLHKGFALALYQTVAVN
YSQPISEASRGSEAINAPGDNPAKVQNHQEPYQAAAAGALTCATPGTWKDRQDGEVLQCMFVCGRPVTPIAQNTTLGSS
RAKLGNFPPWQAFTSIHGRGGGALLGDRWILTAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMCLKGNHPVHRVVVHPDYRQNE
SHNFSGDIALLELQHSIPLGPNVLPVCLPDNETLYRSLGVLGYVSGFGMEMGWLTELKYSRLPVAPREACNAWLQKRQRPVVF
SDNMFVCGDETQRHSVCQDSDGSLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWIKGVMNGKN

An alternative embodiment, FCTR5b, is a 1691 base sequence shown in Table 5C.

Table 5C. FCTR5b Nucleotide Sequence (SEQ ID NO:18)

TTTTTTTTTAAAAAAGGGAAATCCTATTACATCACTGTTGCACCAAGCCACTGCAAGAGAAACCCCCACCC
CCTACCCCAAGTGTTCAGTCTCTCACTCCAGGCCCTCTGTTGCCTGGGGCCTCCACTGTGCTGGTTCAGTCCCTGTTCAGCCCCC
AGGGTCAATTCTTGCCATTCACTCCCTTGATCCAGTCCACATAGCTGAGCACCTTGGTGTAGAAGTCATACCCCTTCGCCA
CACCTTATGCCCCAGGACACAATGCCCGTGGCCACCCAGTGTATGGGCATGATTGTCCCATACCATAGAGGCTGCCACTGTC
CCCCTGGCAGACACTGTGCTTTGCGTCTCATCCCCAACACAGAACATATTGTGAGAAACACCTCGGGTCTCTGTCTCTTTT
GGAGCCAGGCGTTGACAGGCTCCCTGGGAGCTACAGGCAGCCTCGAGTACTTCAGCTCAGTAGTTAGCCAGCCCATCTCCATG
CCAAACCCACTGACGTAGCCCAACAAGCCGCTGCGGTAGAGGCTCTCATTATCGGGCAGACAGACCGGGAGGACGTTGGGGCC
CAGGGGGATGCTGTGCTGCAGTCCAGGAGGCGATGTCCCGCTAAAGTTATGGGACTCATTTCTGACGGTAGTCGGGGTGCA
CAACGACACGGTGGACAGGGTGGTTCCCCAGTTTCAGCATCTCATCTATGGCTGTGTGGCCCAAGAACACATTACACTCTGG
TTCTTCTGAGAGAAACACTGTCTTTGGGGTAGATGGTGTGGGCAGCAGTGAAGATCCATCTGTCCCCAGCAGGGCCCCGCC
CCCACGCGCGTGGTACTGTTGAAGGCTTGCCAGGGGAAGTTGCCAGCTTGGCTCTGGAAGAACCAGGGGTCTGTCTGATTCT
GGGCAATGGGGGTGACTGGCCGTCCGACAGAGGCATACACTGAAGAACCTCTCCCATCTGTCTGTCTTTCCAGGTCCTT
GGGGTTCACAGGTGAGTGGCCCTGTGCTGCGCGGCCTGATAATAGGGCTCTGGCAGTGGTTCTGGACCTTGGCAGGGTTGTC
TCCAGGTGCGTTGATGGCCCTCAGAGCCCTGTGCGCTCGCTGATGGGCTGACTATAGTTACAGCCACGGTTTGGTAGAGGG
CCAGGAAGCCCTTGTGGAGGTGGGCAGTCTTGTCTCCGAGGAAGGCTGTGTGCGGAAGGTGAGCCGCAAACTCCTCCCTGAG
GATACAAACTCCCTCTGACAGGGGGCTGCCAGAGGGGAGCCTTGCTGACCACAGAACTGGCTTGGATCCGAACCGACGAA
TGAGATTGTGACAGAGTCCCTGCACAGTCTGGGACGGCTCCAGGTGCAAGTCTGGAAGACGAGCCTCACAGCAAAGCCCT
CTGGAGCCTTGATGTCCGTGTCTCTCTTGGCCTTTGCCATACGGCTCTGGGTACCCGGGGGATGTGAGCTGCTGGGGTAGC
TCTTGGGCCAAGAGGACGAGCCCGGGTGGGCAAGCCTGGAGGACTCCCAGAGAAGCAGCCACCACATTGCGCCTGGACA
GCCTTTGGAGTGAGGGCTTCTCCAGAGATATTTCCCCACACTCTGGGTCCAGGCATCTGGAACCTGGACATCTGGGACCTGCG
AGAGAACTGGCCAGGATAGGGAACAAAGG

The FCTR5b protein encoded by SEQ ID NO:18 has 487 amino acid residues, and is presented using the one-letter code in Table 5D. FCTR5 was searched against other databases using SignalPep and PSort search protocols. The FCTR5b protein is most likely microbody (peroxisome) (Certainty=0.6406) and seems to have no N-terminal signal sequence. The predicted molecular weight of FCTR5 protein is 53511.9 daltons.

Table 5D. Encoded FCTR5b protein sequence (SEQ ID NO:19).

MPGPRVWGKYLWRSPHSKGCPCGAMWWLLWGVQLQACPTRGSVLLAQELPQQLTSPGYPEPYGKGQESSTDIKAPEGFAVRLVF
QDFDLEPSQDCAGDSVTISFVGSQDPSQFCGQGSPLGRPPGQREFVSSGRSLRLTFRTPQSSSENKTAHLHKGFALALYQTVAVN
YSQPISEASRGSEAINAPGDNPAKVQNHQEPYQAAAAGALTCATPGTWKDRQDGEVLQCMFVCGRPVTPIAQNTTLGSS
RAKLGNFPPWQAFTSIHGRGGGALLGDRWILTAHTIYPKDSVSLRKNQSVNVFLGHTAIDEMCLKGNHPVHRVVVHPDYRQNE

SHNFSGDIALLELQHSIPLGPNVLPVCLPDNETLYRSGLLGYSVSGFGMEMGWLTTTELKYSRLPVAPREACNAWLQKRQRPVEF
SDNMFVCGDETRHSVCQGDGSLYVVDNHAHHWVATGIVSWGIGCGEGYDFYTKVLSYVDWI KGVMMNGKN

The predicted amino acid sequence was searched in the publicly available GenBank
5 database FCTR5a protein showed 58 % identities (177 over 302 amino acids) and 74 %
homologies (226 over 302 amino acids) with human complement C1R component precursor
(EC 3.4.21.41) (705 aa.; ACC:P00736). Based upon homology, FCTR5 proteins and each
homologous protein or peptide may share at least some activity.

In a search of sequence databases, it was found, for example, that the nucleic acid
10 sequence the nucleotides 17-1594 of FCTR5a have 1575 of 1578 bases (99 %) identical to
Homo sapiens complement C1r-like proteinase precursor (GENBANK-ID: XM_007061.1)
(SEQ ID NO:78) (Table 5E).

**Table 5E. BLASTN of FCTR5a against *Homo sapiens* complement C1r-like proteinase
precursor (SEQ ID NO:78)**

15 >GI|11436767|REF|XM_007061.1| HOMO SAPIENS COMPLEMENT C1R-LIKE PROTEINASE
PRECURSOR, (LOC51279),
MRNA
LENGTH = 3318

20 SCORE = 3104 BITS (1566), EXPECT = 0.0
IDENTITIES = 1575/1578 (99%)
STRAND = PLUS / PLUS

25 QUERY: 17 CAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 76
|||||
SBJCT: 1 CAGATGTCCAGTTCAGATGCCTGGACCCAGAGTGTGGGGGAAATATCTCTGGAGAAGCC 60

30 QUERY: 77 CTCACCTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 136
|||||
SBJCT: 61 CTCACCTCCAAAGGCTGTCCAGGCGCAATGTGGTGGCTGCTTCTCTGGGGAGTCCTCCAGG 120

35 QUERY: 137 CTTGCCCAACCCGGGGCTCCGCTCCTCTGGCCCAAGAGCTACCCAGCAGCTGACATCCC 196
|||||
SBJCT: 121 CTTGCCCAACCCGGGGCTCCGCTCCTCTGGCCCAAGAGCTACCCAGCAGCTGACATCCC 180

40 QUERY: 257 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 316
|||||
SBJCT: 241 AGGGCTTTGCTGTGAGGCTCGTCTTCCAGGACTTCGACCTGGAGCCGTCCCAGGACTGTG 300

45 QUERY: 317 CAGGGGACTCTGTACAAATCTCATTCTCGGTTCCGATCCAAGCCAGTTCTGTGGTCAGC 376
|||||
SBJCT: 301 CAGGGGACTCTGTACAAATCTCATTCTCGGTTCCGATCCAAGCCAGTTCTGTGGTCAGC 360

50 QUERY: 377 AAGGCTCCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 436
|||||
SBJCT: 361 AAGGCTCCCCCTCTGGGCAGGCCCCCTGGTCAGAGGGAGTTTGTATCCTCAGGGAGGAGTT 420

55 QUERY: 437 TGC GGCTGACCTTCCGCACACAGCCTTCTCGGAGAACAAAGACTGCCACCTCCACAAGG 496
|||||
SBJCT: 421 TGC GGCTGACCTTCCGCACACAGCCTTCTCGGAGAACAAAGACTGCCACCTCCACAAGG 480

QUERY: 497 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 556
 SBJCT: 481 GCTTCCTGGCCCTCTACCAAACCGTGGCTGTGAACTATAGTCAGCCCATCAGCGAGGCCA 540
 5 QUERY: 557 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACT 616
 SBJCT: 541 GCAGGGGCTCTGAGGCCATCAACGCACCTGGAGACAACCCTGCCAAGGTCCAGAACCACT 600
 10 QUERY: 617 GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGA 676
 SBJCT: 601 GCCAGGAGCCCTATTATCAGGCCGCGGCAGCAGGGGCACTCACCTGTGCAACCCAGGGA 660
 QUERY: 677 CCTGGAAGACAGACAGGATGGGGAGGAGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 736
 15 SBJCT: 661 CCTGGAAGACAGACAGGATGGGGAGGAGTTCTTCAGTGTATGCCTGTCTGCGGACGGC 720
 QUERY: 737 CAGTCACCCCCATTGCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCA 796
 SBJCT: 721 CAGTCACCCCCATTGCCAGAATCAGACGACCCTCGGTTCTTCCAGAGCCAAGCTGGGCA 780
 20 QUERY: 797 ACTTCCCTGGCAAGCCTTACCAGTATCCACGGCCGTGGGGCGGGGCCCTGTGGGGG 856
 SBJCT: 781 ACTTCCCTGGCAAGCCTTACCAGTATCCACGGCCGTGGGGCGGGGCCCTGTGGGGG 840
 25 QUERY: 857 ACAGATGGATCCTCACTGCTGCCACACCATCTACCCAAGGACAGTGTCTCTCAGGA 916
 SBJCT: 841 ACAGATGGATCCTCACTGCTGCCACACCGTCTACCCAAGGACAGTGTCTCTCAGGA 900
 30 QUERY: 917 AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAACTGG 976
 SBJCT: 901 AGAACCAGAGTGTGAATGTGTTCTTGGGCCACACAGCCATAGATGAGATGCTGAACTGG 960
 QUERY: 977 GGAACCACCCTGTCCACCGTGTGTTGTGACCCCGACTACCGTCAGAATGAGTCCATA 1036
 35 SBJCT: 961 GGAACCACCCTGTCCACCGTGTGTTGTGACCCCGACTACCGTCAGAATGAGTCCATA 1020
 QUERY: 1037 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAAG 1096
 SBJCT: 1021 ACTTTAGCGGGGACATCGCCCTCCTGGAGCTGCAGCACAGCATCCCCCTGGGCCCCAAG 1080
 40 QUERY: 1097 TCCTCCCGGTCTGTCTGCCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1156
 SBJCT: 1081 TCCTCCCGGTCTGTCTGCCCCGATAATGAGACCCTCTACCGCAGCGGCTTGTGGGCTACG 1140
 45 QUERY: 1157 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1216
 SBJCT: 1141 TCAGTGGGTTTGGCATGGAGATGGGCTGGCTAACTACTGAGCTGAAGTACTCGAGGCTGC 1200
 50 QUERY: 1217 CTGTAGCTCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1276
 SBJCT: 1201 CTGTAGCTCCAGGGAGGCCTGCAACGCCTGGCTCCAAAAGAGACAGAGACCCGAGGTGT 1260
 QUERY: 1277 TTTCTGACAATATGTTCTGTGTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1336
 55 SBJCT: 1261 TTTCTGACAATATGTTCTGTGTGGGGATGAGACGCAAAGGCACAGTGTCTGCCAGGGGG 1320
 QUERY: 1337 ACAGTGGCAGCCTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1396
 SBJCT: 1321 ACAGTGGCAGCGTCTATGTGGTATGGGACAATCATGCCCATCACTGGGTGGCCACGGGCA 1380
 60 QUERY: 1397 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1456
 SBJCT: 1381 TTGTGTCCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTACACCAAGGTGCTCAGCT 1440
 65 QUERY: 1457 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1516
 SBJCT: 1441 ATGTGGACTGGATCAAGGGAGTGATGAATGGCAAGAATTGACCCTGGGGGCTTGAACAGG 1500

QUERY: 1517 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1576
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 SBJCT: 1501 GACTGACCAGCACAGTGGAGGCCCCAGGCAACAGAGGGCCTGGAGTGAGGACTGAACACT 1560

 5 QUERY: 1577 GGGGTAGGGGGTGGGGGT 1594
 ||||||||| |||||
 SBJCT: 1561 GGGGTAGGGGTGGGGGT 1578

In this search it was also found that the FCTR5a nucleic acid had homology to three
 10 fragments of *Homo sapiens* complement component 1, r subcomponent. It has 102 of 117
 bases (87%) identical to 1458-1574, 82 of 94 bases (87%) identical to 2052-2145, and 54 of
 63 bases (85%) identical to 1678-1740 all fragments of *Homo sapiens* complement
 component 1, r subcomponent (GenBank Acc: NM_001733.1) (Table 5F).

15 **Table 5F. BLASTN of FCTR5a against *Homo sapiens* complement component 1, r
 subcomponent (SEQ ID NO:79)**

>GI|4502492|REF|NM_001733.1| HOMO SAPIENS COMPLEMENT COMPONENT 1, R SUBCOMPONENT
 (C1R), MRNA
 LENGTH = 2386

 20 SCORE = 113 BITS (57), EXPECT = 3E-22
 IDENTITIES = 102/117 (87%)
 STRAND = PLUS / PLUS

 25 QUERY: 783 AGCCAAGCTGGGCAACTTCCCCTGGCAAGCCTTCACCAAGTATCCACGGCCGTGGGGGCGG 842
 ||||||| ||||||||||||||||||| | ||||||| ||||||| || |||||||
 SBJCT: 1458 AGCCAAGATGGGCAACTTCCCCTGGCAGGTGTTACCAACATCCACGGGCGGGGGCGG 1517

 30 QUERY: 843 GGCCCTGTGGGGGACAGATGGATCCTCACTGCTGCCCCACACCATCTACCCCAAGGA 899
 ||||||||||| || | ||||||||||| ||||||||||| | || |||||||
 SBJCT: 1518 GGCCCTGTGGGCGACCGCTGGATCCTCACAGCTGCCACACCCTGTATCCCAAGGA 1574

 SCORE = 91.7 BITS (46), EXPECT = 1E-15
 IDENTITIES = 82/94 (87%)
 35 STRAND = PLUS / PLUS

 40 QUERY: 1380 CTGGGTGGCCACGGGCATTGTGTCTCTGGGGCATAGGGTGTGGCGAAGGGTATGACTTCTA 1439
 ||||||||||||||||| ||||||||||||| ||||| || || ||||| |||||
 SBJCT: 2052 CTGGGTGGCCACGGGCATCGTGTCTCTGGGGCATCGGGTGCAGCAGGGGCTATGGCTTCTA 2111

 45 QUERY: 1440 CACCAAGGTGCTCAGCTATGTGGACTGGATCAAG 1473
 ||||||| ||||||| || |||||||||||||
 SBJCT: 2112 CACCAAAGTGCTCAACTACGTGGACTGGATCAAG 2145

 SCORE = 54.0 BITS (27), EXPECT = 2E-04
 IDENTITIES = 54/63 (85%)
 50 STRAND = PLUS / PLUS

 55 QUERY: 1006 CACCCCGACTACCGTCAGAATGAGTCCCATAACTTTAGCGGGGACATCGCCCTCCTGGAG 1065
 ||||| ||||||||||| ||||||| | || ||| ||||||||||||| |||||
 SBJCT: 1678 CACCCGGACTACCGTCAGGATGAGTCTACAATTTGAGGGGGACATCGCCCTGCTGGAG 1737

 QUERY: 1066 CTG 1068
 |||
 SBJCT: 1738 CTG 1740

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SBJCT: 188 SCQAECSSELYTEASGYISSLEYPRSYPPDLRCNYSIRVERGLTLHLKFLEPFDIDDHQQ 247

QUERY: 94 --CAGDSVTISFVGSQFCGQSGSPLGRPPGQREFVSSGRSLRLTFRTQPSSENKTAH 151

SBJCT: 248 VHCYPYDQLQIYANGKNIGFEFCGKQ-----RPP---DLDTSSNAVDLLFFFTDESQDS----- 295

QUERY: 152 LHKGFALALYQTVAVNYSQP 170

SBJCT: 296 --RGWKLRYTTEIIKCPQP 312

R = AT RESIDUE 46, FCTR5B DIFFERS FROM FCTR5A IN THAT Q46R. THE REST OF THE
HOMOLOGY IS THE SAME.

Based upon homology, FCTR5 proteins and each homologous protein or peptide may
share at least some activity.

FCTR6

The novel nucleic acid of 1078 nucleotides FCTR6a (also designated 27455183.0.19)
encoding a novel human blood coagulation factor XI-like protein is shown in Table 6A. An
ORF was identified beginning with an ATG initiation codon at nucleotides 243-245 and
ending with a TAA codon at nucleotides 1044-1046. A putative untranslated region upstream
from the initiation codon and downstream from the termination codon is underlined in Table
6A, and the start and stop codons are in bold letters.

Table 6A FCTR6a Nucleotide Sequence (SEQ ID NO:20)

TTGATCCGTGCCAAGTGGCTTTTTGTGGGCTCTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCAC
CTCATTTCATATCCCTGGGGCCCCCTGATGGTGAGTGGTCTGGGCTGTGGTCTGCACACCAGCTATTCTGTTTGTGTTTGT
TTTTTTTCTACCTTTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCTTAGAGCTACATGGGAT
TTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCTTCCACTTGCCCTCTCTGGTTCTCTGCCACC
AGTCCAGAAGAACTGAGTGCTGCTGGGGACCAACGACTTAACTAGCCCATCCATGGAATAAAGGAGGTCGCCAGCATCAT
TCTTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCCATCAAGCTCGATGACC
TGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTGCCACATGGCGCGAATGCTGGGTGGCAGGTTGGGGCCAGACCAAT
GCTGCTGACAAAACTCTGTGAAAACGGATCTGATGAAAGTGCCAATGGTTCATCATGGACTGGGAGGAGTGTTCAAAGATGTT
TCCAAAACCTTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGCCCTC
TGGTCTGCACCCAGAGCCTGGTGAGAAGTGGTACCAGGTGGGCATCATCAGCTGGGGAAGAGCTGTGGAGATAAGAACACC
CCAGGGATATACACCTCGTTGGTGAACTACAACCTCTGATCGAGAAAGTGACCCAGCTAGGAGGCAGGCCCTTCAATGCAGA
GAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAGTCTCGGGAGTCCCAGAGCCAGGCAGCCCCAGATCCTGGC
TCCTGCTCTGTCCCTGTCCCATGTGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACCGAAA

The FCTR6a protein encoded by SEQ ID NO:20 has 267 amino acid residues and is
presented using the one-letter code in Table 6B. FCTR6a was searched against other
databases using SignalPep and PSort search protocols. The FCTR6a protein is most likely
mitochondrial matrix space (Certainty= 0.4372) and seems to have no N-terminal signal
sequence. The predicted molecular weight of FCTR6a protein is 29412.8 daltons.

Table 6B. Encoded FCTR6a protein sequence (SEQ ID NO:21).

MGFRFLGTANSATFETSLPLPLAPLWFSATSPPELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLLASPIKL
DDLKVPICLPTQPGPATWRECVAGWGQTNAADKNSVKTDLMKVPVIMDWEECSKMFPKLTKNMLCAGYKNESYDACKGDSG
GPLVCTPEPGEKWKYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEKVTQLGGRPFNAEKRRTSVKQKPMGSPVSGVPEPGSPR
SWLLLCPLSHVLFRAILY

In an alternative embodiment, FCTR6b (alternatively referred to as 27455183.0.145) has the 1334 residue sequence shown in Table 6C. An ORF was identified beginning with an ATG initiation codon at nucleotides 499-501 and ending with a TAA codon at nucleotides 1300-1302. A putative untranslated region upstream from the initiation codon and downstream from the termination codon is underlined in Table 6C, and the start and stop codons are in bold letters.

Table 6C FCTR6b Nucleotide Sequence (SEQ ID NO:22)

GATTTTAGAAGGTTAATCAAAAACCCGGGGACAGTTTCTTCATGGCATAACCACAGACCTTTGTGGCACCCGCTGT
CGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTATTACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTC
TAGACTAACTTCTGGTCTGAGTTCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTAT
CTATCTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTGTGGGCTGTGTAGAGTGCTCTAAACCCAGCTCGGCCTTTG
CTGTATTAGACAGAAGCACCTCATTATATCCCTGGGGCCCCCTGATGGTGCAAGTGGTCTGGCTGTGGTCTGCACACCAGC
TATTCTGTTTTTTTGTGTTTTGTTTTGTTTTTTCCTACCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAG
GGTTTTAAAGGTCCTAGAGCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTCCCC
TTCCACTTGCCCTCTCTGGTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCTGTCTGGGGACCAACGACTTAAGTACG
CCATCCATGGAATAAAGGAGGTGCGCCAGCATCATTCTTACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGC
CTTGCTGTCTGTGGCTTCGCCCATCAAGCTCGATGACCTGAAGGTGCCATCTGCCTCCCCACGCAGCCCGGCTGCCA
CATGGCGCAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGTCTGACAAAACCTCTGTGAAAACGGATCTGATGAAA
GTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAAAGATGTTTCAAACTTACCAAAAATATGCTGTGTGCGCGATA
CAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCAGAGCCTGGTGAGAAGTGGT
ACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCAGGGATATACACCTCGTTGGTGAACCTAC
AACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCAGGCCCTTCAATGCAGAGAGAAAGGAGGACTTCTGTCAAACAGAA
ACCTATGGGCTCCCCAGTCTCGGGAGTCCAGAGCCAGGCAGCCAGATCCTGGCTCCTGTCTGTCCCCTGTCCCATG
TGTTGTTTCAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTTTCAACCGAAA

The FCTR6b protein encoded by SEQ ID NO:22 has 267 amino acid residues and is presented using the one-letter code in Table 6B. The Psort profile for FCTR4 predicts that this sequence has no N-terminal signal peptide and is likely to be localized at the mitochondrial matrix space (Certainty=0.4372). The predicted molecular weight of this protein is 29498.9 Daltons.

Table 6D. Encoded FCTR6b protein sequence (SEQ ID NO:23).

MGFRFLGTANSATFETSLPLPLWFSATSPPELSVVLGTNDLTSPSMEIKEVASIILHKDFKRANMDNDIALLLASPIKL
DDLKVPICLPTQPGPATWRECVAGWGQTNAADKNSVKTDLMKVPMVIMDWEECSKMFPLTKNMLCAGYKNESYDACKGDSG
GPLVCTPEPEKQYQVGIISWKGKSCGEKNTPGIYTSLVNYNLWIEKVTQLEGRPFNAEKRTSVKQKPMGSPVSGVPEPGSPR
SWLLLCPLSHVLFRAILY

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic acid sequence has 853 of 897 bases (95 %) identical to bases 551-1447, and 346 of 388 bases (89%) identical to bases 127-513 of *Macaca fascicularis* brain cDNA, clone QccE-17034 (GENBANK-ID: |AB046651) (Table 6E).

Table 6E. BLASTN of FCTR6a against *Macaca fascicularis* brain cDNA, clone QccE-17034 (SEQ ID NO:82)

>GI|9651112|DBJ|AB046651.1|AB046651 MACACA FASCICULARIS BRAIN CDNA, CLONE QCCE-17034

LENGTH = 1746

SCORE = 1429 BITS (721), EXPECT = 0.0
 IDENTITIES = 853/897 (95%)
 STRAND = PLUS / PLUS

5
 QUERY: 434 CCTTTTCCAATCCTCACACCTTCTGATCAACAGCCCCAGTAGGGTTTAAAGGTCTCTAGA 493
 SBJCT: 551 CCTTTTCCAATCCTCACACCTTCTGAGCTACAGCCCCAGTAGGGTTTAAATGTCTCTAGA 610

10
 QUERY: 494 GCTACATGGGATTTAGGTTTCTGGGCACAGCCAATTCTGCCACTTTTGAGACTTCCCTTC 553
 SBJCT: 611 GCTATATGAGATTTAGGTTTCTGAGCACAGCCAATTCTCCCACTTTTGAGGCTTCCCTTC 670

15
 QUERY: 554 CCCTTCCACTTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAGTGTCTGTGC 613
 SBJCT: 671 CCCTTTCACCTGCCCCCTCTCTGGTTCTCTGCCACCAGTCCAGAAGAACTGAATGTCTGTGC 730

20
 QUERY: 614 TGGGGACCAACGACTTAACTAGCCCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 673
 SBJCT: 731 TGGGGACCAACGACTTAACTAGCTCATCCATGGAAATAAAGGAGGTCGCCAGCATCATTC 790

25
 QUERY: 674 TTCACAAAGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGTCTGTGGCTT 733
 SBJCT: 791 TTCACAAGGACTTTAAGAGAGCCAACATGGACAATGACATTGCCTTGCTGTCTGTGGCCT 850

30
 QUERY: 734 CGCCCATCAAGCTCGATGACCTGAAGGTGCCCATCTGCCTCCCCACGCAGCCCGGCCCTG 793
 SBJCT: 851 CGCCCATCACACTCGATGACCTGAAGGTGCCCATCTGCCTCCCTACGCAGCACGGCCCCG 910

35
 QUERY: 794 CCACATGGCGCAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGTCTGACAAAACT 853
 SBJCT: 911 CCACATGGCACGAATGCTGGGTGGCAGGTTGGGGCCAGACCAATGCTGTCTGACAAAACT 970

40
 QUERY: 854 CTGTGAAAACGGATCTGATGAAAGTGCCAATGGTCATCATGGACTGGGAGGAGTGTTCAA 913
 SBJCT: 971 CTGTGAAAACGGATCTGATGAAAGCGCCGATGGTCATCATGGACTGGGAGGAGTGTTCAA 1030

45
 QUERY: 914 AGATGTTTCCAAAACCTACCAAAAATATGCTGTGTGCCGGATACAAGAATGAGAGCTATG 973
 SBJCT: 1031 AGGCGTTTCCAAAACCTACCAAAAATATGCTGTGTGTGGATACAATAATGAGAGCTATG 1090

50
 QUERY: 974 ATGCCTGCAAGGGTGACAGTGGGGGGCCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1033
 SBJCT: 1091 ACGCCTGCCAGGGTGACAGCGGGGGACCTCTGGTCTGCACCCCAGAGCCTGGTGAGAAGT 1150

55
 QUERY: 1034 GGTACCAGGTGGGCATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1093
 SBJCT: 1151 GGTACCAGGTGGGTATCATCAGCTGGGGAAAGAGCTGTGGAGAGAAGAACACCCCAGGGA 1210

60
 QUERY: 1094 TATACACCTCGTTGGTGAAC TACAACCTCTGGATCGAGAAAGTGACCCAGCTAGAGGGCA 1153
 SBJCT: 1211 TATACACCTCGTTGGTGAAC TACAACCTCTGGATCGAGAAGGTGACCCAGCTAGAGGGCA 1270
 QUERY: 1154 GGCCCTTCAATGCAGAGAAAAGGAGGACTTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1213
 SBJCT: 1271 GGCCCTTCAGTGCAGAGAAAATGAGGACCTCTGTCAAACAGAAACCTATGGGCTCCCCAG 1330

65
 QUERY: 1214 TCTCGGGAGTCCCAGAGCCAGGCGAGCCCCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1273
 SBJCT: 1331 TCTCGGGGGTCCCAGAGCCAGGCGGCCTCAGATCCTGGCTCCTGCTCTGTCCCCTGTCCC 1390

70
 QUERY: 1274 ATGTGTTGTTTCAAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTCTTTCAACC 1330
 SBJCT: 1391 ATGTGTTGTTTCAAGAGCTATTTTGTACTGATAATAAAATAGAGGCTATTTTTTTAACC 1447

75
 SCORE = 428 BITS (216), EXPECT = E-117
 IDENTITIES = 346/388 (89%), GAPS = 1/388 (0%)
 STRAND = PLUS / PLUS

QUERY: 1 GATTTTAGAAGGTTAATCAAAAACCCGGGACAGTTTCTTCATGGCATAACCACAGACCT 60
 |||||
 SBJCT: 127 GATTTTAGAAGGTTAATCAAAAACCCAGGACAGTTTCATCATGTCATAACCAAAGACCC 186

 5 QUERY: 61 TTGTGGCACCCGCTGTCGTGGGATATCAAATATCCTCTGGGGTTCGGAATGTGGGCTTAT 120
 |||||
 SBJCT: 187 TTGTGGCACCTGCTGTCATGGGATAACAAATATCTTGTGGGGTCTGAATGTGGACTTAT 246

 10 QUERY: 121 TACTGAAGATCCTGTCTGCTTGGTCAGTGGCAGGTCTAGACTAACTTCTGGTCCTGAGTT 180
 |||||
 SBJCT: 247 TACTGAAGCTCCTGTCTGCTTGGTCAGTGG-TGGTCTAGACTAACTTCTGGTCCTGAGAT 305

 QUERY: 181 TCTAAAGTGCTGGTAGACCAGTTGATACAAAACAGATATAATAATGAATGCCTTATCTAT 240
 |||||
 15 SBJCT: 306 TCTAAAGTGTGGTAGACCGGTTGAGATAAAAGATATATAATAATGAATGCCTTACCTAT 365

 QUERY: 241 CTGAAGGTCAGTTTGATCCGTGCCAAGTGGCTTTTTGTGGGCTGTGTAGAGTGCTCTAAA 300
 |||||
 20 SBJCT: 366 CTGAAAACAGTTTGATCCGTGCCAAGGGGCTTTTTGTGGGCTCTGTAGAGTGCCCTAAA 425

 QUERY: 301 CCCAGCTCGGCCTTTGCTGTATTAGACAGAAGCACCTCATTTCATATCCCTGGGGCCCTTG 360
 |||||
 SBJCT: 426 CCCAGCTCTGCCTTTGCTGTGTATTAGACAGAAGCACGCCATTACATCTCTGGGGCCCCCA 485

 25 QUERY: 361 ATGGTGCACTGGTCTGGCTGTGGTCTGC 388
 |||||
 SBJCT: 486 ATGGTGCCATGGTGTGGTGTGGTCTGC 513

In a search of sequence databases, it was found, for example, that the FCTR6a nucleic
 acid sequence has 295 of 378 bases (78 %) identical to bases 410-779 of *Mus musculus* adult
 male testis cDNA, RIKEN full-length enriched (GENBANK-ID:AK09660) (Table 6F).

**Table 6F. BLASTN of FCTR6a against *Mus musculus* adult male testis cDNA, RIKEN
 full-length enriched (SEQ ID NO:83)**

>GI|12855429|DBJ|AK016601.1|AK016601 MUS MUSCULUS ADULT MALE TESTIS CDNA, RIKEN
 FULL-LENGTH ENRICHED
 LIBRARY, CLONE:4933401F05, FULL INSERT SEQUENCE
 LENGTH = 1047

 SCORE = 97.6 BITS (49), EXPECT = 2E-17
 IDENTITIES = 295/378 (78%), GAPS = 8/378 (2%)
 STRAND = PLUS / PLUS

 QUERY: 697 AACATGGACAATGACATTGCCTTGCTGCTGCTGGCTTCGCCATCAAGCTCGATGACCTG 756
 |||||
 45 SBJCT: 410 AACATGGACAACGACATTGCCTTGTTGCTGCTAGCCAAGCCCTTGACGTTCAATGAGCTG 469

 QUERY: 757 AAGGTGCCCATCTGCCTCCCCACGCAGCCGCCCTGCCACATGGCGCAATGCTGGGTG 816
 |||||
 50 SBJCT: 470 ACGGTGCCCATCTGCCTTCCTCTCTGGCCCGCCCTCCAGCTGGCAGCAATGCTGGGTG 529

 QUERY: 817 GCAGGTTGGGGCCAGACCAATGCTGCTGACAAAACTCTGTGAAAACGGATCTGATGAAA 876
 |||||
 55 SBJCT: 530 GCAGGATGGGCGTAACCAACTCAACTGACAAGGAATCTATGTCAACGGATCTGATGAAG 589

 QUERY: 877 GTGCCAATGGTCATCATGGAAGTGGGAGGAGTGTCAAAGATGTTTCCAAAACCTTACCAAA 936
 |||||
 SBJCT: 590 GTGCCCATGCGTATCATAGAGTGGGAGGAATGCTTACAGATGTTTCCAGCCTCACCACA 649

 60 QUERY: 937 AATATGCTGTGTGCCGATACAAGAATGAGAGCTATGATGCCTGCAAGGGTGACAGTGGG 996
 |||||
 SBJCT: 650 AACATGCTGTGTGCCTCATATGGTAATGAGAGCTACGATGCTTGC-----CAGTGGG 701

GI|67591|PIR|KQHUP PLASMA KALLIKREIN (EC 3.4.21.34) PRECURSOR - HUMAN
 GI|190263|GB|AAA60153.1| (M13143) PLASMA PREKALLIKREIN [HOMO SAPIENS]
 GI|8809781|GB|AAF79940.1| (AF232742) PLASMA KALLIKREIN PRECURSOR [HOMO SAPIENS]
 LENGTH = 638

SCORE = 133 BITS (334), EXPECT = 3E-30
 IDENTITIES = 80/201 (39%), POSITIVES = 119/201 (58%), GAPS = 18/201 (8%)

QUERY: 20 LPLAPLWFSATSPEELSVVLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLL 77
 ||| +| | +| +|+| +| +||| ||+|+++| + ++|||+|
 SBJCT: 439 LPLQDVW-----RIYSGILNLSDITKDTFPSQIKE---IIHQNYKVSEGNHDIALIKL 489

QUERY: 78 ASPIKLDLKVPICLPTQPGPAT-WRECWVAGWGQTNAADKNSVKTDLMKVPVIMDWEE 136
 +|+ + + |||||++ +| + ||| ||| + +| ++ ||| + ++ ||
 SBJCT: 490 QAPLNYTEFQKPICLPSKGDSTIYTNCWVTGWGFSK--EKGEIQNILQKVNIPLVNTNEE 547

QUERY: 137 CSMKFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKSCGDK 194
 | | + | +| +| +||| | ||||| ||||| + | ||| ||| + | +
 SBJCT: 548 CQKRYQDYKITQRMVCAGYKEGGKDACGDSGGPLVC--KHNGMWRLVGITSWGEGCARR 605

QUERY: 195 NTPGIYTSLVNYNLWIEKVTO 215
 ||+|| + | || + ||
 SBJCT: 606 EQPGVYTKVAEYMDWILEKTQ 626

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 73 of 183 amino acid residues (39%) identical to, and 110 of 183 residues (59%) positive with, the 643 amino acid kallikrein [*Sus scrofa*] (GENBANK-ID:BAA37147.1) (SEQ ID NO:86) (Table 6I).

Table 6I. BLASTP of FCTR6a and b against kallikrein [*Sus scrofa*] (SEQ ID NO:86)

>GI|4165315|DBJ|BAA37147.1| (AB022425) KALLIKREIN [SUS SCROFA]
 LENGTH = 643

SCORE = 128 BITS (322), EXPECT = 9E-29
 IDENTITIES = 73/183 (39%), POSITIVES = 110/183 (59%), GAPS = 12/183 (6%)

QUERY: 38 VLGTNDLT--SPSMEIKEVASIILHKDFKRANMDNDIALLLASPIKLDLKVPICLPTQ 95
 +| +++| +| ++|| |||+|++| +||| | +|+ | + |||||++
 SBJCT: 459 ILNISEITKETPFSQVKE---IIHQNYKILES GHDIALLKLETPLNYTDFQKPICLPSR 515

QUERY: 96 PGP-ATWRECWVAGWGQTNAADKNSVKTDLMKVPVIMDWEECSKMFP--KLTKNMLCAG 152
 + ||| ||| | +| ++ | || + ++ ||| | + |++| | +|||
 SBJCT: 516 DDTNVVYTNWVTGWGFTE--EKGEIQNILQKVNIPVLSNEECQKSYRDHKISKQMICAG 573

QUERY: 153 YKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKSCGDKNTPGIYTSLVNYNLWIEK 212
 || |||||+||| ||| + | + || ||| + | + ||+|| ++ | || +
 SBJCT: 574 YKEGGKDACGESGGPLVC--KYNGIWHLVGTTSWGEGCARREQPGVYTKVIEYMDWILE 631

QUERY: 213 VTQ 215
 ||
 SBJCT: 632 KTQ 634

K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

The FCTR6a amino acid has 81 of 205 amino acid residues (39%) identical to, and 112 of 205 residues (54%) positive with, the 625 amino acid Coagulation factor XI [*Homo sapiens*] (embCAA64368.1) (SEQ ID NO:87) (Table 6J).

**Table 6J. BLASTP of FCTR6a and b against Coagulation factor XI [*Homo sapiens*]
(SEQ ID NO:87)**

```

>GI|180352|GB|AAA51985.1| (M20218) COAGULATION FACTOR XI [HOMO SAPIENS]
    LENGTH = 625

5   SCORE = 127 BITS (320), EXPECT = 1E-28
    IDENTITIES = 81/205 (39%), POSITIVES = 112/205 (54%), GAPS = 17/205 (8%)

10  QUERY: 20  LPLAPLWFSATSPEELSVVLGTNDLTSPSMEIKE-----VASIILHKDFKRANMDNDIA 73
    SBJCT: 427 LTAAHCFYGVESPKILRVYSGILNQS---EIKEDTSFFGVQEIIHDQYKMAESGYDIA 482

15  QUERY: 74  LLLASPIKLDLKVPICLPTQPG-PATWRECWVAGWGQTNAADKNSVKTDLMKVPVMIM 132
    SBJCT: 483 LLKLETTVNYTDSQRPICLPSKGDNRNVIYTDCWVTGWGYRKLKRDK--IQNTLQKAKIPLV 540

20  QUERY: 133 DWEECSKMFP--KLTKNMLCAGYKNESYDACKGDSGGPLVCTPEPGEKQYQVGIISWGKS 190
    SBJCT: 541 TNEECQKRYRGHKITHKMICAGYREGGKDACKGDSGGPLSC--KHNEVWHLVGITSWGEG 598
        K
    QUERY: 191 CGDKNTPGIYTSLVNYNLWIEKVTO 215
    SBJCT: 599 CAQRRERPGVYTNVVEYVDWILEKTQ 623

25  K IS A RESIDUE THAT DIFFERS BETWEEN FCTR6A AND B. D193K.

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The number of new cases of renal cell carcinoma in the United States in 1996 was projected to be 30,600 with an estimated 12,000 deaths. Tumors with a proposed histogenesis from the proximal tubule (clear-cell and chromophilic tumors) amount to 85% of renal cancers, whereas tumors with a proposed histogenesis from the connecting tubule/collecting duct (chromophobic-, oncocytic-, and duct Bellini-type tumors) amount to only 11%.

Adenocarcinomas may be separated into clear cell and granular cell carcinomas, although the 2 cell types may occur together in some tumors. The distinction between well-differentiated renal carcinomas and renal adenomas can be difficult. The diagnosis is usually made arbitrarily on the basis of size of the mass, but size alone should not influence the treatment approach, since metastases can occur with lesions as small as 0.5 centimeters.

While radical nephrectomy with regional lymphadenectomy, is the accepted, often curative therapy for stage I (localized disease) renal cell cancer, very little therapy is available for advance disease that represent about 70% of the patients. Radiotherapy as a postoperative adjuvant has not been effective, and when used preoperatively, may decrease local recurrence but does not appear to improve 5-yr survival. A chemotherapeutic agent capable of significantly altering the course of metastatic renal cell carcinoma has not been identified. (Renal Cell Cancer (PDQ®) Treatment - Health Professionals, Cancernet, NCI)

There is therefore a need to identify genes that are differentially modulated in renal-cell carcinomas. In addition there is a need for methods to assay candidate therapeutic

substances for modulating expression of these genes. These substances might be recombinant protein expressed by the identified genes or antibodies that bind to the identified proteins. There is yet additionally a need for an effective method of identifying target molecules or related components. These and related needs and defects are addressed in the present invention.

Novel kallikrein-like/coagulation factor XI-like Proteins and Nucleic Acids Encoding Same

FCR6 is surprisingly found to be differentially expressed in clear cell Renal cell carcinoma tissues vs the normal adjacent kidney tissues. The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to kallikrein-like, nucleic acids that encode these proteins or fragments thereof, and antibodies that bind immunospecifically to a protein of the invention. It may have use as a therapeutic agent in the treatment of renal cancer and liver cirrhosis.

The utility of kallikrein family members in protein therapy of Renal cancer

The treatment of renal cell carcinoma with recombinant kallikrein could improve disease outcome through several potential mechanisms. The literature suggests that members of this protein family are inhibitory to the process of angiogenesis, a process of vital importance to tumor progression. Renal cell carcinoma is known to be a highly angiogenic cancer. Thus, treatment of renal cell carcinoma with kallikrein may effectively shutdown the active recruitment of a blood supply to a tumor. Members of this protein family are known to play a role in vascular coagulation. Similar to anti-angiogenic therapy, a factor produced by cancer cells that is pro-coagulatory may also act to inhibit cancer growth by effectively “clogging” the tumor vascular supply. In addition, through its proteolytic activity, kallikrein may degrade ECM proteins or growth factors necessary for the progressive growth of cancer cells. Following is a relevant reference underlining the importance of Kallikrein in cancer therapy.

The New Human Kallikrein Gene Family: Implications in Carcinogenesis.

Diamandis EP; Yousef GM; Luo I; Magklara I; Obiezu CV

Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada.

Trends Endocrinol Metab 2000 Mar;11(2):54-60.

ABSTRACT: The traditional human kallikrein gene family consists of three genes, namely KLK1 [encoding human kallikrein 1 (hK1) or pancreatic/renal kallikrein], KLK2 (encoding hK2, previously known as human glandular kallikrein 1) and KLK3 [encoding hK3 or prostate-specific antigen (PSA)]. KLK2 and KLK3 have important applications in prostate cancer diagnostics and, more recently, in breast cancer diagnostics. During the past two to three years, new putative members of the human kallikrein gene family have been identified, including the PRSSL1 gene [encoding normal epithelial cell-specific 1 gene (NES1)], the gene encoding zyme/protease M/neurosin, the gene encoding prostase/KLK-L1, and the genes encoding neuropsin, stratum corneum chymotryptic enzyme and trypsin-like serine protease. Another five putative kallikrein genes, provisionally named KLK-L2, KLK-L3, KLK-L4, KLK-L5 and KLK-L6, have also been identified. Many of the newly identified kallikrein-like genes are regulated by steroid hormones, and a few kallikreins (NES1, protease M, PSA) are known to be downregulated in breast and possibly other cancers. NES1 appears to be a novel breast cancer tumor suppressor protein and PSA a potent inhibitor of angiogenesis. This brief review summarizes recent developments and possible applications of the newly defined and expanded human kallikrein gene locus.

The utility of kallikrein-like/coagulation factor XI-like family members in protein therapy of liver cirrhosis

Results related to inflammation shown below in Example A, Table CC3, panel 4, indicate over-expression of 27455183.0.19 in the liver cirrhosis sample, as compared to panel 1 data (Table CC1), where there is little or no expression in normal adult liver. Panel 4 was generated from various human cell lines that were untreated or resting as well as the same cells that were treated with a wide variety of immune modulatory molecules. There are several disease tissues represented as well as organ controls.

Potential Role(s) of FCTR6 in Inflammation:

Liver cirrhosis occurs in patients with hepatitis C and also in alcoholics. This protein is 41% related to coagulation factor XI and its potential role in liver cirrhosis may be related to cleavage of kininogen. A reference for this follows:

Thromb Haemost 2000 May;83(5):709-14 High molecular weight kininogen is cleaved by FXIa at three sites: Arg409-Arg410, Lys502-Thr503 and Lys325-Lys326. Mauron T, Lammle B, Wuillemin WA Central Hematology Laboratory, University of Bern,

Inselspital, Switzerland.

Abstract:

We investigated the cleavage of high molecular weight kininogen (HK) by activated coagulation factor XI (FXIa) in vitro. Incubation of HK with FXIa resulted in the generation of cleavage products which were subjected to SDS-Page and analyzed by silverstaining, ligand-blotting and immunoblotting, respectively. Upon incubation with FXIa, bands were generated at 111, 100, 88 kDa on nonreduced and at 76, 62 and 51 kDa on reduced gels. Amino acid sequence analysis of the reaction mixtures revealed three cleavage sites at Arg409-Arg410, at Lys502-Thr503 and at Lys325-Lys326. Analysis of HK-samples incubated with FXIa for 3 min, 10 min and 120 min indicated HK to be cleaved first at Arg409-Arg410, followed by cleavage at Lys502-Thr503 and then at Lys325-Lys326. In conclusion, HK is cleaved by FXIa at three sites. Cleavage of HK by FXIa results in the loss of the surface binding site of HK, which may constitute a mechanism of inactivation of HK and of control of contact system activation.

Impact of Therapeutic Targeting of FCTR6 in Inflammation:

Therapeutic targeting of FCTR6 with a monoclonal antibody is anticipated to limit or block the extent of breakdown of kininogen and thereby reduce the degradation of liver that occurs in liver cirrhosis. A pertinent reference is:

Thromb Haemost 1999 Nov;82(5):1428-32 Parallel reduction of plasma levels of high and low molecular weight kininogen in patients with cirrhosis.

Cugno M, Scott CF, Salerno F, Lorenzano E, Muller-Esterl W, Agostoni A, Colman RW
Department of Internal Medicine, IRCCS Maggiore Hospital, University of Milan, Italy.
massimo.cugno@unimi.it

Abstract:

Little is known about the regulation of high-molecular-weight-kininogen (HK) and low-molecular-weight-kininogen (LK) or the relationship of each to the degree of liver function impairment in patients with cirrhosis. In this study, we evaluated HK and LK quantitatively by a recently described particle concentration fluorescence immunoassay (PCFIA) and qualitatively by SDS PAGE and immunoblotting analyses in plasma from 33 patients with cirrhosis presenting various degrees of impairment of liver function. Thirty-three healthy subjects served as normal controls. Patients with cirrhosis had significantly lower plasma levels of HK (median 49 microg/ml [range 22-99 microg/ml]) and LK (58 microg/ml [15-100 microg/ml]) than normal subjects (HK 83 microg/ml [65-115 microg/ml];

LK 80 microg/ml [45-120 microg/ml]) ($p < 0.0001$). The plasma concentrations of HK and LK were directly related to plasma levels of cholinesterase ($P < 0.0001$) and albumin ($P < 0.0001$ and $P < 0.001$) and inversely to the Child-Pugh score ($P < 0.0001$) and to prothrombin time ratio ($P < 0.0001$) (reflecting the clinical and laboratory abnormalities in liver disease). Similar to normal individuals, in patients with cirrhosis, plasma HK and LK levels paralleled one another, suggesting that a coordinate regulation of those proteins persists in liver disease. SDS PAGE and immunoblotting analyses of kininogens in cirrhotic plasma showed a pattern similar to that observed in normal controls for LK (a single band at 66 kDa) with some lower molecular weight forms noted in cirrhotic plasma. A slight increase of cleavage of HK (a major band at 130 kDa and a faint but increased band at 107 kDa) was evident. The increased cleavage of HK was confirmed by the lower cleaved kininogen index (CKI), as compared to normal controls. These data suggest a defect in hepatic synthesis as well as increased destructive cleavage of both kininogens in plasma from patients with cirrhosis. The decrease of important regulatory proteins like kininogens may contribute to the imbalance in coagulation and fibrinolytic systems, which frequently occurs in cirrhotic patients.

In summary, the differential expression of FCTR6 (Kallikrein family) in renal cell carcinoma is an important finding that could have immense potential in renal carcinogenesis. In addition, overexpression of the above gene in liver cirrhosis demonstrates its anticipated use as an immunotherapeutic target.

FCTR7

The novel nucleic acid of 1498 nucleotides FCTR7 (also designated. 32592466.0.64) encoding a novel trypsin inhibitor-like protein is shown in Table 7A. An ORF begins with an ATG initiation codon at nucleotides 470-472 and ends with a TAA codon at nucleotides 1369-1371. Putative untranslated regions, if any, are found upstream from the initiation codon and downstream from the termination codon.

Table 7A. FCTR7 Nucleotide Sequence (SEQ ID NO:24)

AGGCGCCTGGTTCTGCGCGTACTGGCTGTACGGAGCAGGAGCAAGAGGTGCGCCGCCAGCCTCCGCCGCCGAGCCTCGTTTCGTG
TCCCCGCCCTCGCTCCTGCAGCTACTGCTCAGAAACGCTGGGGCGCCACCTGGCAGACTAACGAAGCAGCTCCCTTCCCA
CCCCAACTGCAGGTCTAATTTGGACGCTTTGCCTGCCATTTCTCCAGGTTGAGGGAGCCGAGAGGCGGAGGCTCGCGTAT
TCCTGCAGTCAGCACCCACGTGCGCCCCGGACGCTCGGTGCTCAGGCCCTTCGCGAGCGGGGCTCTCCGTCTGCGGTCCCTTG
TGAAGGCTCTGGGCGGCTGCAGAGGCGGCCGCTCCGGTTTGGCTCACCTCTCCAGGAACTTCACACTGGAGAGCCAAAAGG
AGTGAAGAGCCTGTCTTGAGATTTTCTGGGAAATCCTGAGGTCATTATTGAAGTGTACCGCGCGGAGTGGCTCAG
AGTAACCACAGTGTGTTTCATGGCTAGAGCAATTCAGCCATGGTGGTTCCCAATGCCACTTTATTGGAGAACTTTGGAAA
AATACATGGATGAGGATGGTGGTGGATAGCCAAACAACGAGGGAAAGGGCCATCACAGACAATGACATGCAGAGTATT
TTGGACCTTCATAATAAATTACGAAGTCAGGTGTATCCAACAGCCTCTAATATGGAGTATATGACATGGGATGTAGAGCTGGA
AAGATCTGCAGAATCCAGGGCTGAAATTGCTTGTGGGAACATGGACCTGCAAGCTTGCTTCCATCAATTGGACAGAATTTGGG

AGCACACTGGGGAAGATATAGGCCCCGACGTTTCATGTACAATCGTGGTATGATGAAGTGAAAGACTTTAGCTACCCATATG
AACATGAATGCAACCCATATTGTCCATTAGGTGTTCTGGCCCTGTATGTACACATTATACACAGGTCGTGTGGGCAACTAGT
AACAGAATCGGTTGTGCCATTAAATTTGTGTCATAACATGAACATCTGGGGGCAGATATGGCCCAAAGCTGTCTACCTGGTGTG
CAATTACTCCCCAAAGGGAACTGGTGGGGCCATGCCCTTACAAACATGGGCGGCCCTGTTCTGCTTGCCCACTAGTTTTG
GAGGGGGCTGTAGAGAAAATCTGTGCTACAAAGAAGGGTCAGACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATGAAATA
GAACGGCAGCAGTCACAAGTCCATGACACCCATGTCCGGACAAGATCAGATGATAGTAGCAGAAATGAAGTCATTAGCTTTGG
GAAAAGTAATGAAAATATAATGGTTTTAGAAATCCTGTGTTAAATATTGCTATATTTTCTAGCAGTTATTTCTACAGTTAAT
TACATAGTCATGATTGTTCTACGTTTCATATATTATATGGTGCTTTGTATATGCCCTAATAAAATGAATCTAAACATTGAAA
AAAA

The FCTR7 protein encoded by SEQ ID NO:24 has 300 amino acid residues and is presented using the one-letter code in Table 7B. The FCTR7 gene was found to be expressed in: brain; germ cell tumors. FCTR7 gene maps to Unigene cluster Hs.182364 which is expressed in the following tissues: brain, breast, ear, germ cell, heart, liver, lung, whole embryo, ovary, pancreas, pooled, prostate, stomach, testis, uterus, vascular. Therefore the FCTR7 protein described in this invention is also expressed in the above tissues.

The SignalP, Psort and/or Hydropathy profile for FCTR7 predict that this sequence has a signal peptide and is likely to be localized outside of the cell with a certainty of 0.4228. The SignalP shows a cleavage site between amino acids 20 and 21, *i.e.*, at the dash in the sequence amino acid ARA-IP. The predicted molecular weight of FCTR7 is 34739.9 Daltons. Hydropathy profile shows an amino terminal hydrophobic region. This region could function as a signal peptide and target the invention to be secreted or plasma membrane localized.

Table 7B. Encoded FCTR7 protein sequence (SEQ ID NO:25).

MKCTAREWLVRTTVLFMARAI PAMVVPNATLLEKLLLEKYMDEDGEWIIAKQGRKRAITDNDMQSILDLHNKLRSQVYPTASNM
EYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCT
HYTQVWVATSNRIGCAINLCHNMNIWGQIWPKAIVLVCNYSKGNWNGHAPYKHGRPCACPPSFGGGCRENL CYKEGSDRY
PPREETNEIERQQSQVHDTHVTRSDSSRNEVISFGKSNENIMVLEILC

This gene maps to Unigene cluster Hs.182364 which has been assigned the following mapping information shown in table 7C. Therefore the chromosomal assignment for this gene is the same as that for Unigene cluster 182364.

Table 7C. Mapping Information.

Chromosome:	8
Gene Map 98:	Marker SHGC-32056 , Interval D8S279-D8S526
Gene Map 98:	Marker SGC32056 , Interval D8S526-D8S275
Gene Map 98:	Marker sts-G20223 , Interval D8S526-D8S275
Gene Map 98:	Marker stSG30385 , Interval D8S526-D8S275
Whitehead map:	EST67946, Chr.8
dbSTS entries:	G25853, G29349, G20223

The predicted amino acid sequence was searched in the publicly available GenBank

database

FCTR7 protein showed Score = 743 (261.5 bits), Expect = 1.4e-73, P = 1.4e-73, 54 % identities (129 over 237 amino acids) and 43% homologies (167 over 237 amino acids) with human 25 kD trypsin inhibitor protein (258 aa; ACC:O43692) (Table 7D).

Table 7D. BLAST X search results are shown below:

```
ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - HO... +2 743 8.4e-73 1
(SEQ ID NO:88)
ptnr:SPTREMBL-ACC:O44228 HRTT-1 - HALOCYNTHIA RORETZI ... +2 325 2.9e-28 1
(SEQ ID NO:89)
ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED ... +2 314 5.3e-27 1
(SEQ ID NO:90)
ptnr:PIR-ID:JC4131 glioma pathogenesis-related protein... +2 309 2.0e-26 1
(SEQ ID NO:91)
ptnr:SWISSNEW-ACC:O19010 CYSTEINE-RICH SECRETORY PROTE... +2 258 9.4e-21 1
(SEQ ID NO:92)
```

The nucleotide sequence of FCTR7 has 954 of 957 residues (99 %) identical to the 1-957 base segment, and 174 of 175 residues (99%) identical to bases 1317-1953 of the 2664 nucleotide *Homo sapiens* putative secretory protein precursor, mRNA (GenBank-ACC: AF142573) (SEQ ID NO:93) (Table 7E).

Table 7E. BLASTN of FCTR7 against Putative secretory protein precursor (SEQ ID NO:93)

```
>gi|12002310|gb|AF142573.1|AF142573 Homo sapiens putative secretory protein
precursor, mRNA, complete cds
Length = 2664

Score = 1865 bits (941), Expect = 0.0
Identities = 954/957 (99%), Gaps = 1/957 (0%)
Strand = Plus / Plus

Query: 364 gtccgggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag
423
Sbjct: 1 |||||gtccgggtttggctcacctctcccaggaaacttcacactggagagccaaaaggagtggaag 60

Query: 424 agcctgtcttggagattttcctggggaaatcctgaggtcattcattatgaagtgtaccgc
483
Sbjct: 61 |||||agcctgtcttggagattttcctggggaaatcctgaggtcattcattatgaagtgtaccgc
120

Query: 484 gcgggagtggtcagagtaaccacagtgtgttcatggctagagcaattccagccatggt
543
```


Sbjct: 721 ttactccccaagggaaactggtggggccatgcccttacaaacatgggcggcctgttc
780

5 Query: 1143 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc
1202
|||||
Sbjct: 781 tgcttgcccacctagttttggagggggctgtagagaaaatctgtgctacaaagaagggtc
840

10 Query: 1203 agacagggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca
1262
|||||
Sbjct: 841 agacagggtattatccccctcgagaagaggaaacaaatgaaatagaacggcagcagtcaca
900

15 Query: 1263 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 1319
|||||
Sbjct: 901 agtccatgacacccatgtccggacaagatcagatgatagtagcagaaatgaagtcac 957

20 Score = 339 bits (171), Expect = 3e-90
Identities = 174/175 (99%)
Strand = Plus / Plus

25 Query: 1317 cattagctttgggaaaagtaatgaaaatataatgggttttagaaatcctgtgttaaatt
1376
|||||
Sbjct: 1779 cattagctttgggaaaagtaatgaaaatataatgggttttagaaatcctgtgttaaatt
1838

30 Query: 1377 gctatattttcttagcagttattttctacagttaattacatagtcattgttctacgtt
1436
|||||
Sbjct: 1839 gctatattttcttagcagttattttctacagttaattacatagtcattgttctacgtt
1898

35 Query: 1437 tcatatatttatatggtgctttgtatatgccctaataaaatgaatctaaacattg 1491
|||||
Sbjct: 1899 tcatatatttatatggtgctttgtatatgccctaataaaatgaatctaaacattg 1953

40 The FCTR7 amino acid has 284 of 285 amino acid residues (99%) identical to, and
284 of 285 amino acid residues (99%) similar to, the 500 amino acid Putative secretory
protein precursor [*Homo sapiens*] (GenBank-Acc No.: AF142573) (SEQ ID NO:94) (Table
7F).

**Table 7F. BLASTP alignments of FCTR7 against Putative secretory protein precursor,
(SEQ ID NO:94)**

>gi|12002311|gb|AAG43287.1|AF142573_1 (AF142573) putative secretory protein
precursor [*Homo sapiens*]
Length = 500

50 Score = 581 bits (1499), Expect = e-165
Identities = 284/285 (99%), Positives = 284/285 (99%)

Query: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60
|||||
55 Sbjct: 1 MKCTAREWLRVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDGEWWIAKQRGKRAITDN 60

```

Query: 61      DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESRAESCLWEHG PASLLPSIGQNL 120
          |||
Sbjct: 61      DMQSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESWAESCLWEHG PASLLPSIGQNL 120
          |||

Query: 121     GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIG 180
          |||
Sbjct: 121     GAHWGRYRPPTFHVQSWYDEVKDFSYPYEHECNPYCPFRCSGPVCTHYTQVVWATSNRIG 180
          |||

Query: 181     CAINLCHNMNIWGQIWPKAVYLVCNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL C 240
          |||
Sbjct: 181     CAINLCHNMNIWGQIWPKAVYLVCNYS PKGNWWGHAPYKHGRPCSACPPSFGGGCRENL C 240
          |||

Query: 241     YKEGSDRYYP PREEETNEIERQOSQVHDTHVRTRSDSSRNEVIS 285
          |||
Sbjct: 241     YKEGSDRYYP PREEETNEIERQOSQVHDTHVRTRSDSSRNEVIS 285
          |||

```

The FCTR7 amino acid has 137 of 176 amino acid residues (78%) identical to, and 151 of 176 amino acid residues (86%) similar to, the 188 amino acid Late gestation lung protein 1 [*Rattus norvegicus*] (GenBank-Acc No.: AF109674) (SEQ ID NO:95) (Table 7G).

>gi|4324682|gb|AAD16986.1| (AF109674) late gestation lung protein 1 [Rattus norvegicus]

Query: 68 LHNKLR SQVYPTASNM EYMTWDV ELERSAESRAESCLWEHG PASLLPSIGQNLGAHWGRY 127
 ||||| |||| ||||||| ||||| | ||||||| |||||
 Sbjct: 2 LHNKLRGQVYPPASNM EYMTWDEELERSAAAWAORCLWEHG PASLLVSGONLAVHWGRY 61

Query: 128 RPPTFHVQSWYDEVKDFSPYPEHECNPYCPFRCSGPVCTHYTQVWVATSNRIGCAINLCH 187
| | | | | | | | | | ++ | | | | | + | | | | + | | | | + | | | | + | | | | ++ |
Sbjct: 62 RSPGFHVQSWYDEVKDYTYPYPHECNPWCPERCSGAMCTHYTOMVWATTNKIGCAVHTCR 121

Query: 188 NMNIWGQIWP KAVYLVCNYS PKGNWGHAPYKHGRPCSACPPSFGGGCRENL CYKE 243
 + ||+|| || ||||| ||||| || ||||| || || ||||| || || ||||| ||||| + ||||| ||||| +
 Sbjct: 122 SMSVWGD I WENAVYLVCNYS PKGNWIG EAPYKHGRPCSECPSSYGGGCRNNLCYRE 177

The FCTR7 amino acid has 130 of 237 amino acid residues (55%) identical to, and 165 of 237 amino acid residues (70%) similar to, the 258 amino acid R3H domain-containing preproprotein; 25 kDa trypsin inhibitor [*Homo sapiens*] (GenBank-Acc No.: D45027) (SEQ ID NO:96) (Table 7H).

Table 7H. BLASTP alignments of FCTR7 against R3H domain-containing preproprotein, 25 kDa trypsin inhibitor (SEO ID NO:96)

```
>gi|7705676|ref|NP_056970.1| R3H domain-containing preproprotein; 25 kDa
trypsin inhibitor; R3H
        domain (binds single-stranded nucleic acids) containing
        [Homo sapiens]
```

gi|2943716|dbj|BAA25066.1| (D45027) 25 kDa trypsin inhibitor [*Homo sapiens*]

Length = 258

5 Score = 265 bits (678), Expect = 4e-70
Identities = 130/237 (55%), Positives = 165/237 (70%), Gaps = 3/237 (1%)

Query: 12 TTVLFMARAIPAMVVPNATLLEKLLEKYMDEDEGEWWIAKQRGKRAITDNDMQSILDLHNK 71
+||+ + + | | +| + +| | | | | + ||| +||| ||+
10 Sbjct: 20 STVVLLNSTDSSPPTNNFTDIEAALKAQLDSAD---IPKARRKRYISQNDMIAILDYHNQ 76

Query: 72 LRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRPPT 131
+| +|+| +||| | | | | | | +|+||| + | +||| | | | |
15 Sbjct: 77 VRGKVFPFAANMEYMWVDENLAKSAEAWAATCIWDHGPSYLLRFLGQNLVVRTGRYSIL 136

Query: 132 FHVQSWYDEVKDFSYPYEHECNPYCFRCSGPVCTHYTQVWATSNRIGCAINLCHNMNI 191
| + ||||| |+++| +||| | | | | +||| | +||| | | | | + | | | +
20 Sbjct: 137 QLVKPYDEVKDYAFYPQDCNPRCPMRCFGPMCTHYTQMVWATSNRIGCAIHTCQNMNV 196

Query: 192 WGQIWPKAVYLVLCNYSPKGNWWGHAPYKHGRPCACPPSFGGGCRENL CYKEGSDRY 248
|| +| +||| | | +||| | | | | | | +||| +|| | +||| + + |
25 Sbjct: 197 WGSVWRRAYLVLCNYAPKGNWIGEAPYKVGVPSCSPSYGGSCDNLCPFGVTSNY 253

The FCTR7 amino acid has 109 of 233 amino acid residues (47%) identical to, and
25 146 of 233 amino acid residues (63%) similar to, the 253 amino acid Novel protein similar to
a trypsin inhibitor [*Homo sapiens*] 25 kDa trypsin inhibitor (EMBLAcc No.: AL117382)
(SEQ ID NO:97) (Table 7I).

Table 7I. BLASTP alignments of FCTR7 against Novel protein similar to a trypsin inhibitor, (SEQ ID NO:97)

30 >gi|9885193|emb|CAC04190.1| (AL117382) dJ881L22.3 (novel protein similar to
a trypsin inhibitor) [*Homo sapiens*]
35 Length = 253

Score = 225 bits (575), Expect = 4e-58
Identities = 109/233 (47%), Positives = 146/233 (63%), Gaps = 8/233 (3%)

40 Query: 10 RVTTVLFMARAIPAMVVPNATLLEKLLEKYMDEDEGEWWIAKQRGKRAITDNDMQSILDLH 69
+ | | | | | +| + | + + | | | + | | ++| |
Sbjct: 19 QAVNALIMPATPAPAQPESTAMRL-----SGLEVPRYRRKRHISVRDMNALLDYH 70

45 Query: 70 NKLRSQVYPTASNMEYMTWDVELERSAESRAESCLWEHGPASLLPSIGQNLGAHWGRYRP 129
| +|+ ||| +||| | | | | | | +| ||| +| + +||| | | +||
Sbjct: 71 NHIRASVYPPAANMEYMWVDKRLARAAEAWATQCIWAHGSQLMRYVGQNL SIHSGQYRS 130

Query: 130 PTFHVQSWYDEVKDFSYPYEHECNPYCFRCSGPVCTHYTQVWATSNRIGCAINLCHNM 189
++|| +| + +| +||| +||| | | +||| +||| +||| +||| + | ++
50 Sbjct: 131 VVDLMKSWSEEKWHYLFAPRDCNPHCPWRCDGPTCSHYTQMVWASSNRLGCAIHTCSSI 190

Query: 190 NIWGQIWPKAVYLVLCNYSPKGNWWGHAPYKHGRPCACPPSFGGGCRENL CYK 242
++|| | +| ||||| + |||| | +||| +||| +||| + | | +|+|
55 Sbjct: 191 SVWGNTWHRAAYLVLCNYAIKGNWIGESPYKMGKPCSSCPPSYQGSCNSNMCFK 243

The FCTR7 amino acid has 129 of 237 amino acid residues (54%) identical to, and 167 of 237 amino acid residues (70%) similar to, the 258 amino acid 25 kDa Trypsin Inhibitor from *Homo sapiens* (EMBLAcc No.: O43692) (SEQ ID NO:88) (Table 7J).

Table 7J. BLASTP alignments of FCTR7 against 25 kDa Trypsin Inhibitor, (SEQ ID NO:88)

ptnr:SPTREMBL-ACC:O43692 25 KDA TRYPSIN INHIBITOR - *Homo sapiens* (Human), 258 aa.

Score = 743 (261.5 bits), Expect = 1.6e-73, P = 1.6e-73
Identities = 129/237 (54%), Positives = 167/237 (70%)

The FCTR7 amino acid has 79 of 193 amino acid residues (40%) identical to, and 110 of 193 amino acid residues (56%) similar to, the 266 amino acid Glioma Pathogenesis-Related Protein (RTVP-1 Protein) - *Homo sapiens* (SWISSPROT Acc No.: P48060) (SEQ ID NO:90) (Table 7K).

Table 7K. BLASTP alignments of FCTR7 against Glioma Pathogenesis-Related Protein, (SEQ ID NO:90)

ptnr:SWISSPROT-ACC:P48060 GLIOMA PATHOGENESIS-RELATED PROTEIN (RTVP-1 PROTEIN) - *Homo sapiens* (Human), 266 aa

Score = 314 (110.5 bits), Expect = 4.7e-28, P = 4.7e-28
Identities = 79/193 (40%), Positives = 110/193 (56%)

The FCTR7 amino acid has 66 of 186 amino acid residues (35%) identical to, and 91 of 186 amino acid residues (48%) similar to, the 186 amino acid Neutrophil granules matrix glycoprotein SGP28 precursor from *Homo sapiens* (SWISSPROT Acc No.: S68691) (SEQ ID NO:98) (Table 7L).

Table 7L. BLASTP alignments of FCTR7 against Neutrophil granules matrix glycoprotein, (SEQ ID NO:98)

ptnr:PIR-ID:S68691 neutrophil granules matrix glycoprotein SGP28 precursor - human

Score = 254 (89.4 bits), Expect = 1.1e-21, P = 1.1e-21
Identities = 66/186 (35%), Positives = 91/186 (48%)

A novel developmentally regulated gene with homology to a tumor derived trypsin inhibitor is expressed in lung mesenchyme, as described in Am. J. Physiol. 0:0-0(1999). cDNA cloning of a novel trypsin inhibitor with similarity to pathogenesis-related proteins, and its frequent expression in human brain cancer cells is disclosed in Biochim. Biophys.

Acta 1395:202-208(1998). RTVP-1, a novel human gene with sequence similarity to genes of diverse species, is expressed in tumor cell lines of glial but not neuronal origin, as published in Gene 180:125-130(1996). The human glioma pathogenesis-related protein is structurally related to plant pathogenesis-related proteins and its gene is expressed specifically in brain tumors (Gene 159:131-135(1995)). Structure comparison of human glioma pathogenesis-related protein GliPR and the plant pathogenesis-related protein P14a indicates a functional link between the human immune system and a plant defense system (Proc. Natl. Acad. Sci. U.S.A. 95:2262-2266(1998)). GliPR is highly expressed in the human brain tumor, glioblastoma multiform/astrocytoma, but neither in normal fetal or adult brain tissue, nor in other nervous system tumors. GliPR belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1. SGP28, a novel matrix glycoprotein in specific granules of human neutrophils with similarity to a human testis-specific gene product and to a rodent sperm-coating glycoprotein (FEBS Lett. 380, 246-250, 1996). The primary structure and properties of helothermine, a peptide toxin that blocks ryanodine receptors is described in Biophys. J. 68:2280-2288(1995). As GliPR, Helothermine belongs to a family that groups mammalian SCP/TPX1; insects AG3/AG5; FUNGI SC7/SC14 and plants PR-1.

Based upon homology, FCTR7 protein and each homologous protein or peptide may share at least some activity.

Therapeutic uses:

FCTR7 protein has homology to trypsin inhibitors, Q91055 helothermine, tumor derived trypsin inhibitors, glioma pathogenesis-related protein, Q9Z0U6 LATE GESTATION LUNG PROTEIN 1, and to the Prosite family which groups mammalian SCP/TPX1;INSECTS AG3/AG5; FUNGI SC7/SC14 AND PLANTS PR-1 proteins. Therefore the FCTR7 protein disclosed in this invention could function like the proteins which it has homology to. These functions include tissue development *in vitro* and *in vivo*, and cancer pathogenesis.

Based the tissue expression pattern, the gene is implicated in diseases of tissues in which it is expressed. These diseases include but are not limited to:

- Glioma,
- cancer,
- lung diseases,

- gestation,
- male and female reproductive diseases,
- deafness,
- neurological disorders,
- gastric disorders, and
- pancreatic diseases like diabetes.

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel FCTR7 substances for use in therapeutic or diagnostic methods. These antibodies may be generated according to methods known in the art, using prediction from hydrophobicity charts, as described in the “Anti-FCTR7 Antibodies” section below. In one embodiment, a contemplated FCTR7 epitope is from aa 40 to 120. In another embodiment, a FCTR7 epitope is from aa 130 to 170. In additional embodiments, FCTR7 epitopes are from aa 210 to 230, and from aa 240 to 280.

TABLE 8A: Summary Of Nucleic Acids And Proteins Of The Invention

Name	Tables	Clone; Description of Homolog	Nucleic Acid SEQ ID NO	Amino Acid SEQ ID NO
FCTR1	1A, 1B,	58092213.0.36 follistatin-like protein	1	2
FCTR2	2A, 2B	AC012614_1.0.123; KIAA1061-like protein	3	4
FCTR3	3A, 3B	10129612.0.118; neurestin-like protein	5	6
	3C, 3D	10129612.0.405; neurestin-like protein	7	8
	3E	10129612.0.154; neurestin-like protein	9	
	3F	10129612.0.67; neurestin-like protein	10	
	3G	10129612.0.258; neurestin-like protein	11	
	3H, 3I	10129612.0.352; neurestin-like protein	12	13
FCTR4	4A, 4B	29692275.0.1; NF-Kappa-B P65delta3-like protein	14	15
FCTR5	5A, 5B	32125243.0.21; human complement C1R component precursor -like protein	16	17
	5C, 5D		18	19
FCTR6	6A, 6B	27455183.0.19; novel human blood coagulation factor XI -like protein	20	21
	6C, 6D	27455183.0.145; novel human blood coagulation factor XI -like protein	22	23
FCTR7	7A, 7B	32592466.0.64; trypsin inhibitor -like protein	24	25
FCTR1	Example 2	Ag809 Forward	26	
FCTR1	Example 2	Ag809 Probe	27	
FCTR1	Example 2	Ag809 Reverse	28	
FCTR4	Example 2	Ag2773 Forward	29	
FCTR4	Example 2	Ag2773 Probe	30	

FCTR4	Example 2	Ag2773 Reverse	31	
FCTR5	Example 2	Ag427 Forward	32	
FCTR5	Example 2	Ag427 Probe	33	
FCTR5	Example 2	Ag427 Reverse	34	
FCTR6	Example 2	Ag1541 Forward	35	
FCTR6	Example 2	Ag1541 Probe	36	
FCTR6	Example 2	Ag1541 Reverse	37	

TABLE 8B: Summary of Query Sequences Disclosed

Table	Database	Acc. No.	Sequence Name	Species	SEQ ID NO.
1C, 1K	remtrEmbl	BAA21725	IGFBP-like protein	mouse	38
1D	sptrEmbl	Q61581	Follistatin-like protein-2	Mouse	39
1E	SptrEmbl	Q07822	Mac25 protein	Human	40
1F, 1K	SptrEmbl	O88812	Mac25 protein	Mouse	41
1G, 1K	SptrEmbl	Q16270	Prostacyclin-stimulating factor	Human	42
1H, 1K	PIR	B40098	Colorectal cancer suppressor	Rat	43
1I	TrEmblnew	AAD9360	PTP sigma (brain) precursor	Human	44
1J	SptrEmbl	Q13332	PTP sigma precursor	Human	45
2C	GenBank	AB028984	KIAA1061 cDNA	Human	46
2D	TrEmblnew	BAA85677	KIAA1263	Human	47
2E	TrEmblnew	BAA83013	KIAA1061 protein fragment	Human	48
2F	Embl	CAB70877.1	Hypothetical protein DKFzp566D234.1	Human	49
2G	GenBank	Q62632	Follistatin-related protein-1 precursor	Rat	50
2H	GenBank	Q62536	Follistatin-related protein-1 precursor	Mouse	51
2I	GenBank	JG0187	Follistatin related protein	African clawed frog	52
2J	GenBank	Q12841	Follistatin related protein-1 precursor	Human	53
2K	Embl	CAB42968.1	Flik protein	Chicken	54
2L	GenBank	T13822	Frazzled gene protein	Fruit fly	55
2M	GenBank	AAC38849.1	Roundabout 1	Fruit fly	56
2N	GenBank	O60469	Down Syndrome Cell Adhesion Molecule Precursor	Human	57
2O	SwissProt	Q13449	Limbic system-associated membrane protein precursor	Human	58
2P	SptrEmbl	O70246	Putative neuronal cell adhesion molecule, short form	Mouse	59
2Q	SptrEmbl	O02869	CHLAMP, G11-isoform precursor	Chicken	60
2R	SwissProt	Q62813	Limbic system-associated membrane protein precursor	Rat	61
3J	GenBank	NM_011856.2	Odd Oz/ten-m homology 2	Fruit fly	62
3K	Embl	AJ245711.1	Teneurin-2 cDNA, short splice variant	Chicken	63
3L	GenBank	AB032953	KIAA 1127 cDNA	Human	64

3M, 3U	GenBank	AB025411	Ten-m2 cDNA	Mouse	65
3N	GenBank	NM_020088.1	Neurestin alpha cDNA	Rat	66
3O	Embl	GGA278031	Teneurin-2	Chicken	67
3P	GenBank	NP_035986.2	Odd Oz/ten-m homology 2	Fruit fly	68
3Q	Embl	CAC09416.1	Teneurin-2	Chicken	69
3R	GenBank	BAA77399.1	Ten-m4	Mouse	70
3S	GenBank	AB032953	KIAA1127 protein	Human	71
3T	GenBank	AF086607	Neurestin alpha	Rat	72
4C	SpnrEmbl	Q99233	Hypothetical 10 kD protein	Trypanosome	73
4C	SpnrEmbl	Q16896	GABA receptor subunit		74
4C	SpnrEmbl	O76473	GABA receptor subunit		75
4C	TrEmblnew	AAD28317	FI3J11.13 protein		76
Text p. 90	SpnrEmbl	Q13313	NF-kappa B P65 delta 3 protein	Human	77
5E	GenBank	XM_007061.1	Complement C1R-like proteinase precursor	Human	78
5F	GenBank	NM_001733.1	Complement component 1, R subcomponent cDNA	Human	79
5G	GenBank	AAF44349.1	Complement C1R-like proteinase precursor	Human	80
5H	GenBank	AAA5185.1	Complement C1R component precursor	Human	81
6E	GenBank	AB046651	Brain cDNA clone Qcc-17034	Macaque	82
6F	GenBank	AK09660	Adult testis cDNA, RIKEN full length enriched	Mouse	83
6G	GenBank	AB046651	Hypothetical protein	Macaque	84
6H	GenBank	NP_000838.1	Plasma kallikrein B1 precursor	Human	85
6I	GenBank	BAA37147.1	Kallikrein	Pig	86
6J	Embl	CAA64368.1	Coagulation factor XI	Human	87
7D, 7J	SpnrEmbl	O43692	25 kDa trypsin inhibitor	Human	88
7D	SpnrEmbl	O44228	HRTT-1		89
7D, 7K	SpnrEmbl	P418060	Glioma pathogenesis-related protein	Human	90
7D	PIR-ID	JC4131	Glioma pathogenesis-related protein	Human	91
7D	SwissProt	O19010	Cysteine-rich secretory protein		92
7E	GenBank	AF142573	Putative secretory protein precursor cDNA	Human	93
7F	GenBank	AF142573	Putative secretory protein precursor	Human	94
7G	GenBank	AF109674	Late gestation lung protein 1	Rat	95
7H	GenBank	D45027	R3H domain containing preprotein, 25 kDa trypsin inhibitor	Human	96
7I	Embl	AL117382	Novel protein similar to a trypsin inhibitor	Human	97
7L	PIR-ID	S68691	Neutrophil granules matrix glycoprotein SGP28 precursor	Human	98

FCRX Nucleic Acids and Polypeptides

One aspect of the invention pertains to isolated nucleic acid molecules that encode FCRX polypeptides or biologically-active portions thereof. Also included in the invention are nucleic acid fragments sufficient for use as hybridization probes to identify FCRX-
5 encoding nucleic acids (*e.g.*, FCRX mRNAs) and fragments for use as PCR primers for the amplification and/or mutation of FCRX nucleic acid molecules. As used herein, the term “nucleic acid molecule” is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof. The nucleic acid
10 molecule may be single-stranded or double-stranded, but preferably is comprised double-stranded DNA.

An FCRX nucleic acid can encode a mature FCRX polypeptide. As used herein, a “mature” form of a polypeptide or protein disclosed in the present invention is the product of a naturally occurring polypeptide or precursor form or proprotein. The naturally occurring
15 polypeptide, precursor or proprotein includes, by way of nonlimiting example, the full length gene product, encoded by the corresponding gene. Alternatively, it may be defined as the polypeptide, precursor or proprotein encoded by an ORF described herein. The product “mature” form arises, again by way of nonlimiting example, as a result of one or more naturally occurring processing steps as they may take place within the cell, or host cell, in
20 which the gene product arises. Examples of such processing steps leading to a “mature” form of a polypeptide or protein include the cleavage of the N-terminal methionine residue encoded by the initiation codon of an ORF, or the proteolytic cleavage of a signal peptide or leader sequence. Thus a mature form arising from a precursor polypeptide or protein that has residues 1 to N, where residue 1 is the N-terminal methionine, would have residues 2 through
25 N remaining after removal of the N-terminal methionine. Alternatively, a mature form arising from a precursor polypeptide or protein having residues 1 to N, in which an N-terminal signal sequence from residue 1 to residue M is cleaved, would have the residues from residue M+1 to residue N remaining. Further as used herein, a “mature” form of a polypeptide or protein may arise from a step of post-translational modification other than a
30 proteolytic cleavage event. Such additional processes include, by way of non-limiting example, glycosylation, myristoylation or phosphorylation. In general, a mature polypeptide or protein may result from the operation of only one of these processes, or a combination of any of them.

The term "probes", as utilized herein, refers to nucleic acid sequences of variable length, preferably between at least about 10 nucleotides (nt), 100 nt, or as many as approximately, *e.g.*, 6,000 nt, depending upon the specific use. Probes are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are generally obtained from a natural or recombinant source, are highly specific, and much slower to hybridize than shorter-length oligomer probes. Probes may be single- or double-stranded and designed to have specificity in PCR, membrane-based hybridization technologies, or ELISA-like technologies.

The term "isolated" nucleic acid molecule, as utilized herein, is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5'- and 3'-termini of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated FCYTRX nucleic acid molecules can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell/tissue from which the nucleic acid is derived (*e.g.*, brain, heart, liver, spleen, etc.). Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material or culture medium when produced by recombinant techniques, or of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement of this aforementioned nucleotide sequence, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24 as a hybridization probe, FCYTRX molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, *et al.*, (eds.), MOLECULAR CLONING: A LABORATORY MANUAL 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989; and Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993.)

A nucleic acid of the invention can be amplified using cDNA, mRNA or alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore,

oligonucleotides corresponding to FCTRX nucleotide sequences can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

As used herein, the term “oligonucleotide” refers to a series of linked nucleotide residues, which oligonucleotide has a sufficient number of nucleotide bases to be used in a PCR reaction. A short oligonucleotide sequence may be based on, or designed from, a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue.

Oligonucleotides comprise portions of a nucleic acid sequence having about 10 nt, 50 nt, or 100 nt in length, preferably about 15 nt to 30 nt in length. In one embodiment of the invention, an oligonucleotide comprising a nucleic acid molecule less than 100 nt in length would further comprise at least 6 contiguous nucleotides of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a complement thereof. Oligonucleotides may be chemically synthesized and may also be used as probes.

In another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule that is a complement of the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion of this nucleotide sequence (*e.g.*, a fragment that can be used as a probe or primer or a fragment encoding a biologically-active portion of an FCTRX polypeptide). A nucleic acid molecule that is complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, is one that is sufficiently complementary to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that it can hydrogen bond with little or no mismatches to the nucleotide sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby forming a stable duplex.

As used herein, the term “complementary” refers to Watson-Crick or Hoogsteen base pairing between nucleotides units of a nucleic acid molecule, and the term “binding” means the physical or chemical interaction between two polypeptides or compounds or associated polypeptides or compounds or combinations thereof. Binding includes ionic, non-ionic, van der Waals, hydrophobic interactions, and the like. A physical interaction can be either direct or indirect. Indirect interactions may be through or due to the effects of another polypeptide or compound. Direct binding refers to interactions that do not take place through, or due to, the effect of another polypeptide or compound, but instead are without other substantial chemical intermediates.

Fragments provided herein are defined as sequences of at least 6 (contiguous) nucleic acids or at least 4 (contiguous) amino acids, a length sufficient to allow for specific

hybridization in the case of nucleic acids or for specific recognition of an epitope in the case of amino acids, respectively, and are at most some portion less than a full length sequence. Fragments may be derived from any contiguous portion of a nucleic acid or amino acid sequence of choice. Derivatives are nucleic acid sequences or amino acid sequences formed from the native compounds either directly or by modification or partial substitution. Analogs are nucleic acid sequences or amino acid sequences that have a structure similar to, but not identical to, the native compound but differs from it in respect to certain components or side chains. Analogs may be synthetic or from a different evolutionary origin and may have a similar or opposite metabolic activity compared to wild type. Homologs are nucleic acid sequences or amino acid sequences of a particular gene that are derived from different species.

Derivatives and analogs may be full length or other than full length, if the derivative or analog contains a modified nucleic acid or amino acid, as described below. Derivatives or analogs of the nucleic acids or proteins of the invention include, but are not limited to, molecules comprising regions that are substantially homologous to the nucleic acids or proteins of the invention, in various embodiments, by at least about 70%, 80%, or 95% identity (with a preferred identity of 80-95%) over a nucleic acid or amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art, or whose encoding nucleic acid is capable of hybridizing to the complement of a sequence encoding the aforementioned proteins under stringent, moderately stringent, or low stringent conditions. See *e.g.* Ausubel, *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, New York, NY, 1993, and below.

A "homologous nucleic acid sequence" or "homologous amino acid sequence," or variations thereof, refer to sequences characterized by a homology at the nucleotide level or amino acid level as discussed above. Homologous nucleotide sequences encode those sequences coding for isoforms of FCNTRX polypeptides. Isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. In the invention, homologous nucleotide sequences include nucleotide sequences encoding for an FCNTRX polypeptide of species other than humans, including, but not limited to: vertebrates, and thus can include, *e.g.*, frog, mouse, rat, rabbit, dog, cat, cow, horse, and other organisms. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous

nucleotide sequence does not, however, include the exact nucleotide sequence encoding human FCTR_X protein. Homologous nucleic acid sequences include those nucleic acid sequences that encode conservative amino acid substitutions (see below) in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, as well as a polypeptide possessing FCTR_X biological activity. Various biological activities of the FCTR_X proteins are described below.

An FCTR_X polypeptide is encoded by the open reading frame ("ORF") of an FCTR_X nucleic acid. An ORF corresponds to a nucleotide sequence that could potentially be translated into a polypeptide. A stretch of nucleic acids comprising an ORF is uninterrupted by a stop codon. An ORF that represents the coding sequence for a full protein begins with an ATG "start" codon and terminates with one of the three "stop" codons, namely, TAA, TAG, or TGA. For the purposes of this invention, an ORF may be any part of a coding sequence, with or without a start codon, a stop codon, or both. For an ORF to be considered as a good candidate for coding for a *bona fide* cellular protein, a minimum size requirement is often set, *e.g.*, a stretch of DNA that would encode a protein of 50 amino acids or more.

The nucleotide sequences determined from the cloning of the human FCTR_X genes allows for the generation of probes and primers designed for use in identifying and/or cloning FCTR_X homologues in other cell types, *e.g.* from other tissues, as well as FCTR_X homologues from other vertebrates. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 25, 50, 100, 150, 200, 250, 300, 350 or 400 consecutive sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or an anti-sense strand nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24; or of a naturally occurring mutant of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

Probes based on the human FCTR_X nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In various embodiments, the probe further comprises a label group attached thereto, *e.g.* the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express an FCTR_X protein, such as by measuring a level of an FCTR_X-encoding nucleic acid in a sample of cells from a subject *e.g.*, detecting FCTR_X mRNA levels or determining whether a genomic FCTR_X gene has been mutated or deleted.

"A polypeptide having a biologically-active portion of an FCTR_X polypeptide" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a

polypeptide of the invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. A nucleic acid fragment encoding a "biologically-active portion of FCTR_X" can be prepared by isolating a portion of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, that encodes a polypeptide having an FCTR_X biological activity (the biological activities of the FCTR_X proteins are described below), expressing the encoded portion of FCTR_X protein (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of FCTR_X.

FCTR_X Nucleic Acid and Polypeptide Variants

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, due to degeneracy of the genetic code and thus encode the same FCTR_X proteins as that encoded by the nucleotide sequences shown in SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

In addition to the human FCTR_X nucleotide sequences shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the FCTR_X polypeptides may exist within a population (*e.g.*, the human population). Such genetic polymorphism in the FCTR_X genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame (ORF) encoding an FCTR_X protein, preferably a vertebrate FCTR_X protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the FCTR_X genes. Any and all such nucleotide variations and resulting amino acid polymorphisms in the FCTR_X polypeptides, which are the result of natural allelic variation and that do not alter the functional activity of the FCTR_X polypeptides, are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding FCTR_X proteins from other species, and thus that have a nucleotide sequence that differs from the human sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the FCTR_X cDNAs of the invention can be isolated based on their homology to the human

FCTRX nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 6 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24. In another embodiment, the nucleic acid is at least 10, 25, 50, 100, 250, 500, 750, 1000, 1500, or 2000 or more nucleotides in length. In yet another embodiment, an isolated nucleic acid molecule of the invention hybridizes to the coding region. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other.

Homologs (*i.e.*, nucleic acids encoding FCTRX proteins derived from species other than human) or other related sequences (*e.g.*, paralogs) can be obtained by low, moderate or high stringency hybridization with all or a portion of the particular human sequence as a probe using methods well known in the art for nucleic acid hybridization and cloning.

As used herein, the phrase "stringent hybridization conditions" refers to conditions under which a probe, primer or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter sequences. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present at excess, at T_m, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (*e.g.*, 10 nt to 50 nt) and at least about 60°C for longer probes, primers and oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

Stringent conditions are known to those skilled in the art and can be found in Ausubel, *et al.*, (eds.), CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, N.Y.

(1989), 6.3.1-6.3.6. Preferably, the conditions are such that sequences at least about 65%, 70%, 75%, 85%, 90%, 95%, 98%, or 99% homologous to each other typically remain hybridized to each other. A non-limiting example of stringent hybridization conditions are hybridization in a high salt buffer comprising 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm DNA at 65°C, followed by one or more washes in 0.2X SSC, 0.01% BSA at 50°C. An isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (*e.g.*, encodes a natural protein).

In a second embodiment, a nucleic acid sequence that is hybridizable to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of moderate stringency is provided. A non-limiting example of moderate stringency hybridization conditions are hybridization in 6X SSC, 5X Denhardt's solution, 0.5% SDS and 100 mg/ml denatured salmon sperm DNA at 55°C, followed by one or more washes in 1X SSC, 0.1% SDS at 37°C. Other conditions of moderate stringency that may be used are well-known within the art. See, *e.g.*, Ausubel, et al. (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990; GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY.

In a third embodiment, a nucleic acid that is hybridizable to the nucleic acid molecule comprising the nucleotide sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof, under conditions of low stringency, is provided. A non-limiting example of low stringency hybridization conditions are hybridization in 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 mg/ml denatured salmon sperm DNA, 10% (wt/vol) dextran sulfate at 40°C, followed by one or more washes in 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS at 50°C. Other conditions of low stringency that may be used are well known in the art (*e.g.*, as employed for cross-species hybridizations). See, *e.g.*, Ausubel, et al. (eds.), 1993, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, NY, and Kriegler, 1990, GENE TRANSFER AND EXPRESSION, A LABORATORY MANUAL, Stockton Press, NY; Shilo and Weinberg, 1981. *Proc Natl Acad Sci USA* 78: 6789-6792.

Conservative Mutations

In addition to naturally-occurring allelic variants of FCTR_X sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, thereby leading to changes in the amino acid sequences of the encoded FCTR_X proteins, without altering the functional ability of said FCTR_X proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequences of the FCTR_X proteins without altering their biological activity, whereas an "essential" amino acid residue is required for such biological activity. For example, amino acid residues that are conserved among the FCTR_X proteins of the invention are predicted to be particularly non-amenable to alteration. Amino acids for which conservative substitutions can be made are well-known within the art.

Another aspect of the invention pertains to nucleic acid molecules encoding FCTR_X proteins that contain changes in amino acid residues that are not essential for activity. Such FCTR_X proteins differ in amino acid sequence from SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet retain biological activity. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 45% homologous to the amino acid sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. Preferably, the protein encoded by the nucleic acid molecule is at least about 60% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; more preferably at least about 70% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; still more preferably at least about 80% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; even more preferably at least about 90% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; and most preferably at least about 95% homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

An isolated nucleic acid molecule encoding an FCTR_X protein homologous to the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein.

Mutations can be introduced into SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, by standard techniques, such as site-directed mutagenesis and PCR-mediated

mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted, non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined within the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted non-essential amino acid residue in the FCTR_X protein is replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an FCTR_X coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for FCTR_X biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, the encoded protein can be expressed by any recombinant technology known in the art and the activity of the protein can be determined.

The relatedness of amino acid families may also be determined based on side chain interactions. Substituted amino acids may be fully conserved "strong" residues or fully conserved "weak" residues. The "strong" group of conserved amino acid residues may be any one of the following groups: STA, NEQK, NHQK, NDEQ, QHRK, MILV, MILF, HY, FYW, wherein the single letter amino acid codes are grouped by those amino acids that may be substituted for each other. Likewise, the "weak" group of conserved residues may be any one of the following: CSA, ATV, SAG, STNK, STPA, SGND, SNDEQK, NDEQHK, NEQHRK, VLIM, HFY, wherein the letters within each group represent the single letter amino acid code.

In one embodiment, a mutant FCTR_X protein can be assayed for (i) the ability to form protein:protein interactions with other FCTR_X proteins, other cell-surface proteins, or biologically-active portions thereof, (ii) complex formation between a mutant FCTR_X protein and an FCTR_X ligand; or (iii) the ability of a mutant FCTR_X protein to bind to an intracellular target protein or biologically-active portion thereof; (*e.g.* avidin proteins).

In yet another embodiment, a mutant FCTR_X protein can be assayed for the ability to regulate a specific biological function (*e.g.*, regulation of insulin release).

Antisense Nucleic Acids

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein (*e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence). In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire FCTR_X coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of an FCTR_X protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25; or antisense nucleic acids complementary to an FCTR_X nucleic acid sequence of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an FCTR_X protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the FCTR_X protein. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding the FCTR_X protein disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of FCTR_X mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of FCTR_X mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of FCTR_X mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally-occurring nucleotides or

variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids (*e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used).

5 Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine,
10 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil,
15 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense
20 orientation to a target nucleic acid of interest, described further in the following subsection).

 The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an FCTR_X protein to thereby inhibit expression of the protein (*e.g.*, by inhibiting transcription and/or translation). The hybridization can be by conventional
25 nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site.

 Alternatively, antisense nucleic acid molecules can be modified to target selected cells and
30 then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface (*e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens). The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve

5 sufficient nucleic acid molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other. See, e.g., Gaultier, *et al.*, 1987. *Nucl. Acids Res.* **15**: 6625-6641. The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (see, e.g., Inoue, *et al.* 1987. *Nucl. Acids Res.* **15**: 6131-6148) or a chimeric RNA-DNA analogue (see, e.g., Inoue, *et al.*, 1987. *FEBS Lett.* **215**: 327-330).

10 **Ribozymes and PNA Moieties**

Nucleic acid modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject.

In one embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes as described in Haselhoff and Gerlach 1988. *Nature* 334: 585-591) can be used to catalytically cleave FCTR_X mRNA transcripts to thereby inhibit translation of FCTR_X mRNA. A ribozyme having specificity for an FCTR_X-encoding nucleic acid can be designed based upon the nucleotide sequence of an FCTR_X cDNA disclosed herein (*i.e.*, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an FCTR_X-encoding mRNA. See, e.g., U.S. Patent 4,987,071 to Cech, *et al.* and U.S. Patent 5,116,742 to Cech, *et al.* FCTR_X mRNA can also be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, FCTR_X gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the FCTR_X nucleic acid (e.g., the FCTR_X promoter and/or enhancers) to form triple helical structures that prevent transcription

of the FCTR_X gene in target cells. See, e.g., Helene, 1991. *Anticancer Drug Des.* 6: 569-84; Helene, *et al.* 1992. *Ann. N.Y. Acad. Sci.* 660: 27-36; Maher, 1992. *Bioassays* 14: 807-15.

In various embodiments, the FCTR_X nucleic acids can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids. See, e.g., Hyrup, *et al.*, 1996. *Bioorg Med Chem* 4: 5-23. As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics (e.g., DNA mimics) in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained.

The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup, *et al.*, 1996. *supra*; Perry-O'Keefe, *et al.*, 1996. *Proc. Natl. Acad. Sci. USA* 93: 14670-14675.

PNAs of FCTR_X can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of FCTR_X can also be used, for example, in the analysis of single base pair mutations in a gene (e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S₁ nucleases (see, Hyrup, *et al.*, 1996. *supra*); or as probes or primers for DNA sequence and hybridization (see, Hyrup, *et al.*, 1996, *supra*; Perry-O'Keefe, *et al.*, 1996. *supra*).

In another embodiment, PNAs of FCTR_X can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of FCTR_X can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes (e.g., RNase H and DNA polymerases) to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (see, Hyrup, *et al.*, 1996. *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup, *et al.*, 1996. *supra* and Finn, *et al.*, 1996. *Nucl Acids Res* 24: 3357-3363. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, e.g., 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine

phosphoramidite, can be used between the PNA and the 5' end of DNA. *See, e.g., Mag, et al., 1989. Nucl Acid Res* 17: 5973-5988. PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment. *See, e.g., Finn, et al., 1996. supra.* Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. *See, e.g., Petersen, et al., 1975. Bioorg. Med. Chem. Lett.* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.,* for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (*see, e.g., Letsinger, et al., 1989. Proc. Natl. Acad. Sci. U.S.A.* 86: 6553-6556; Lemaitre, *et al., 1987. Proc. Natl. Acad. Sci.* 84: 648-652; PCT Publication No. WO88/09810) or the blood-brain barrier (*see, e.g.,* PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (*see, e.g., Krol, et al., 1988. BioTechniques* 6:958-976) or intercalating agents (*see, e.g., Zon, 1988. Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.,* a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, and the like.

FCTR_X Polypeptides

A polypeptide according to the invention includes a polypeptide including the amino acid sequence of FCTR_X polypeptides whose sequences are provided in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residues shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, while still encoding a protein that maintains its FCTR_X activities and physiological functions, or a functional fragment thereof.

In general, an FCTR_X variant that preserves FCTR_X-like function includes any variant in which residues at a particular position in the sequence have been substituted by other amino acids, and further include the possibility of inserting an additional residue or residues between two residues of the parent protein as well as the possibility of deleting one or more residues from the parent sequence. Any amino acid substitution, insertion, or deletion is encompassed by the invention. In favorable circumstances, the substitution is a conservative substitution as defined above.

One aspect of the invention pertains to isolated FCTR_X proteins, and biologically-active portions thereof, or derivatives, fragments, analogs or homologs thereof. Also provided are polypeptide fragments suitable for use as immunogens to raise anti-FCTR_X

antibodies. In one embodiment, native FCTR_X proteins can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, FCTR_X proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, an FCTR_X protein or polypeptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the FCTR_X protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of FCTR_X proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the language "substantially free of cellular material" includes preparations of FCTR_X proteins having less than about 30% (by dry weight) of non-FCTR_X proteins (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-FCTR_X proteins, still more preferably less than about 10% of non-FCTR_X proteins, and most preferably less than about 5% of non-FCTR_X proteins. When the FCTR_X protein or biologically-active portion thereof is recombinantly-produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the FCTR_X protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of FCTR_X proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of FCTR_X proteins having less than about 30% (by dry weight) of chemical precursors or non-FCTR_X chemicals, more preferably less than about 20% chemical precursors or non-FCTR_X chemicals, still more preferably less than about 10% chemical precursors or non-FCTR_X chemicals, and most preferably less than about 5% chemical precursors or non-FCTR_X chemicals.

Biologically-active portions of FCTR_X proteins include peptides comprising amino acid sequences sufficiently homologous to or derived from the amino acid sequences of the FCTR_X proteins (*e.g.*, the amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25) that include fewer amino acids than the full-length FCTR_X proteins, and exhibit at least one activity of an FCTR_X protein. Typically, biologically-active portions

comprise a domain or motif with at least one activity of the FCTR_X protein. A biologically-active portion of an FCTR_X protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acid residues in length.

Moreover, other biologically-active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native FCTR_X protein.

In an embodiment, the FCTR_X protein has an amino acid sequence shown in SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25. In other embodiments, the FCTR_X protein is substantially homologous to SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the protein of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, yet differs in amino acid sequence due to natural allelic variation or mutagenesis, as described in detail, below. Accordingly, in another embodiment, the FCTR_X protein is a protein that comprises an amino acid sequence at least about 45% homologous to the amino acid sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and retains the functional activity of the FCTR_X proteins of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25.

Determining Homology Between Two or More Sequences

To determine the percent homology of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are homologous at that position (*i.e.*, as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity").

The nucleic acid sequence homology may be determined as the degree of identity between two sequences. The homology may be determined using computer programs known in the art, such as GAP software provided in the GCG program package. *See*, Needleman and Wunsch, 1970. *J Mol Biol* 48: 443-453. Using GCG GAP software with the following settings for nucleic acid sequence comparison: GAP creation penalty of 5.0 and GAP extension penalty of 0.3, the coding region of the analogous nucleic acid sequences referred to above exhibits a degree of identity preferably of at least 70%, 75%, 80%, 85%, 90%, 95%,

98%, or 99%, with the CDS (encoding) part of the DNA sequence shown in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24.

The term "sequence identity" refers to the degree to which two polynucleotide or polypeptide sequences are identical on a residue-by-residue basis over a particular region of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over that region of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I, in the case of nucleic acids) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the region of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The term "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 80 percent sequence identity, preferably at least 85 percent identity and often 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison region.

Chimeric and Fusion Proteins

The invention also provides FCTR_X chimeric or fusion proteins. As used herein, an FCTR_X "chimeric protein" or "fusion protein" comprises an FCTR_X polypeptide operatively-linked to a non-FCTR_X polypeptide. An "FCTR_X polypeptide" refers to a polypeptide having an amino acid sequence corresponding to an FCTR_X protein (SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25), whereas a "non-FCTR_X polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein that is not substantially homologous to the FCTR_X protein, *e.g.*, a protein that is different from the FCTR_X protein and that is derived from the same or a different organism. Within an FCTR_X fusion protein the FCTR_X polypeptide can correspond to all or a portion of an FCTR_X protein. In one embodiment, an FCTR_X fusion protein comprises at least one biologically-active portion of an FCTR_X protein. In another embodiment, an FCTR_X fusion protein comprises at least two biologically-active portions of an FCTR_X protein. In yet another embodiment, an FCTR_X fusion protein comprises at least three biologically-active portions of an FCTR_X protein. Within the fusion protein, the term "operatively-linked" is intended to indicate that the FCTR_X polypeptide and the non-FCTR_X polypeptide are fused in-frame with one another. The non-FCTR_X polypeptide can be fused to the N-terminus or C-terminus of the FCTR_X polypeptide.

In one embodiment, the fusion protein is a GST-FCTR_X fusion protein in which the FCTR_X sequences are fused to the C-terminus of the GST (glutathione S-transferase) sequences. Such fusion proteins can facilitate the purification of recombinant FCTR_X polypeptides.

5 In another embodiment, the fusion protein is an FCTR_X protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression and/or secretion of FCTR_X can be increased through use of a heterologous signal sequence.

10 In yet another embodiment, the fusion protein is an FCTR_X-immunoglobulin fusion protein in which the FCTR_X sequences are fused to sequences derived from a member of the immunoglobulin protein family. The FCTR_X-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between an FCTR_X ligand and an FCTR_X protein on the surface of a cell, to thereby suppress FCTR_X-mediated signal transduction *in vivo*. The FCTR_X-
15 immunoglobulin fusion proteins can be used to affect the bioavailability of an FCTR_X cognate ligand. Inhibition of the FCTR_X ligand/FCTR_X interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, as well as modulating (*e.g.* promoting or inhibiting) cell survival. Moreover, the FCTR_X-immunoglobulin fusion proteins of the invention can be used as immunogens to
20 produce anti-FCTR_X antibodies in a subject, to purify FCTR_X ligands, and in screening assays to identify molecules that inhibit the interaction of FCTR_X with an FCTR_X ligand.

An FCTR_X chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional
25 techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene
30 fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (*see, e.g.*, Ausubel, *et al.* (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). An

FCTR_X-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the FCTR_X protein.

FCTR_X Agonists and Antagonists

The invention also pertains to variants of the FCTR_X proteins that function as either FCTR_X agonists (*i.e.*, mimetics) or as FCTR_X antagonists. Variants of the FCTR_X protein can be generated by mutagenesis (*e.g.*, discrete point mutation or truncation of the FCTR_X protein). An agonist of the FCTR_X protein can retain substantially the same, or a subset of, the biological activities of the naturally occurring form of the FCTR_X protein. An antagonist of the FCTR_X protein can inhibit one or more of the activities of the naturally occurring form of the FCTR_X protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the FCTR_X protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. In one embodiment, treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein has fewer side effects in a subject relative to treatment with the naturally occurring form of the FCTR_X proteins.

Variants of the FCTR_X proteins that function as either FCTR_X agonists (*i.e.*, mimetics) or as FCTR_X antagonists can be identified by screening combinatorial libraries of mutants (*e.g.*, truncation mutants) of the FCTR_X proteins for FCTR_X protein agonist or antagonist activity. In one embodiment, a variegated library of FCTR_X variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of FCTR_X variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential FCTR_X sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display) containing the set of FCTR_X sequences therein. There are a variety of methods which can be used to produce libraries of potential FCTR_X variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential FCTR_X sequences. Methods for synthesizing degenerate oligonucleotides are well-known within the art. *See, e.g.*, Narang, 1983. *Tetrahedron* 39: 3; Itakura, *et al.*, 1984. *Annu. Rev. Biochem.* 53: 323; Itakura, *et al.*, 1984. *Science* 198: 1056; Ike, *et al.*, 1983. *Nucl. Acids Res.* 11: 477.

Polypeptide Libraries

In addition, libraries of fragments of the FCTR_X protein coding sequences can be used to generate a variegated population of FCTR_X fragments for screening and subsequent selection of variants of an FCTR_X protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an FCTR_X coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S₁ nuclease, and ligating the resulting fragment library into an expression vector. By this method, expression libraries can be derived which encodes N-terminal and internal fragments of various sizes of the FCTR_X proteins.

Various techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of FCTR_X proteins. The most widely used techniques, which are amenable to high throughput analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique that enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify FCTR_X variants. See, e.g., Arkin and Yourvan, 1992. *Proc. Natl. Acad. Sci. USA* 89: 7811-7815; Delgrave, et al., 1993. *Protein Engineering* 6:327-331.

Anti-FCTR_X Antibodies

The invention encompasses antibodies and antibody fragments, such as F_{ab} or (F_{ab})₂, that bind immunospecifically to any of the FCTR_X polypeptides of said invention.

An isolated FCTR_X protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind to FCTR_X polypeptides using standard techniques for polyclonal and monoclonal antibody preparation. The full-length FCTR_X proteins can be used or, alternatively, the invention provides antigenic peptide fragments of FCTR_X proteins for use as immunogens. The antigenic FCTR_X peptides comprises at least 4

amino acid residues of the amino acid sequence shown in SEQ ID NO NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, and encompasses an epitope of FCTR_X such that an antibody raised against the peptide forms a specific immune complex with FCTR_X. Preferably, the antigenic peptide comprises at least 6, 8, 10, 15, 20, or 30 amino acid residues. Longer antigenic peptides are sometimes preferable over shorter antigenic peptides, depending on use and according to methods well known to someone skilled in the art.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of FCTR_X that is located on the surface of the protein (*e.g.*, a hydrophilic region). As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation (*see, e.g.*, Hopp and Woods, 1981. *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle, 1982. *J. Mol. Biol.* 157: 105-142, each incorporated herein by reference in their entirety).

As disclosed herein, FCTR_X protein sequences of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or derivatives, fragments, analogs or homologs thereof, may be utilized as immunogens in the generation of antibodies that immunospecifically-bind these protein components. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically-active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically-binds (immunoreacts with) an antigen, such as FCTR_X. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab} and F_{(ab)²} fragments, and an F_{ab} expression library. In a specific embodiment, antibodies to human FCTR_X proteins are disclosed. Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies to an FCTR_X protein sequence of SEQ ID NOS:2, 4, 6, 8, 13, 15, 17, 19, 21, 23, and 25, or a derivative, fragment, analog or homolog thereof. Some of these proteins are discussed below.

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by injection with the native protein, or a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed FCTR_X protein or a chemically-synthesized FCTR_X polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide),

surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as *Bacille Calmette-Guerin* and *Corynebacterium parvum*, or similar immunostimulatory agents. If desired, the antibody molecules directed against FCTR_X can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as protein A chromatography to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of FCTR_X. A monoclonal antibody composition thus typically displays a single binding affinity for a particular FCTR_X protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular FCTR_X protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (see, e.g., Kohler & Milstein, 1975. *Nature* 256: 495-497); the trioma technique; the human B-cell hybridoma technique (see, e.g., Kozbor, *et al.*, 1983. *Immunol. Today* 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see, e.g., Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the invention and may be produced by using human hybridomas (see, e.g., Cote, *et al.*, 1983. *Proc Natl Acad Sci USA* 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus *in vitro* (see, e.g., Cole, *et al.*, 1985. In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Each of the above citations is incorporated herein by reference in their entirety.

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an FCTR_X protein (see, e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see, e.g., Huse, *et al.*, 1989. *Science* 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for an FCTR_X protein or derivatives, fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. See, e.g., U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotypes to an FCTR_X protein may be produced by techniques known in the art including, but not limited to: (i) an F_(ab)₂ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an

F_{(ab)₂} fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent; and (iv) F_v fragments.

Additionally, recombinant anti-FCTR_X antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; U.S. Pat. No. 5,225,539; European Patent Application No. 125,023; Better, *et al.*, 1988. *Science* 240: 1041-1043; Liu, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 3439-3443; Liu, *et al.*, 1987. *J. Immunol.* 139: 3521-3526; Sun, *et al.*, 1987. *Proc. Natl. Acad. Sci. USA* 84: 214-218; Nishimura, *et al.*, 1987. *Cancer Res.* 47: 999-1005; Wood, *et al.*, 1985. *Nature* 314 :446-449; Shaw, *et al.*, 1988. *J. Natl. Cancer Inst.* 80: 1553-1559; Morrison(1985) *Science* 229:1202-1207; Oi, *et al.* (1986) *BioTechniques* 4:214; Jones, *et al.*, 1986. *Nature* 321: 552-525; Verhoevan, *et al.*, 1988. *Science* 239: 1534; and Beidler, *et al.*, 1988. *J. Immunol.* 141: 4053-4060. Each of the above citations are incorporated herein by reference in their entirety.

In one embodiment, methods for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art. In a specific embodiment, selection of antibodies that are specific to a particular domain of an FCTR_X protein is facilitated by generation of hybridomas that bind to the fragment of an FCTR_X protein possessing such a domain. Thus, antibodies that are specific for a desired domain within an FCTR_X protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

Anti-FCTR_X antibodies may be used in methods known within the art relating to the localization and/or quantitation of an FCTR_X protein (*e.g.*, for use in measuring levels of the FCTR_X protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for FCTR_X proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody derived binding domain, are utilized as pharmacologically-active compounds (hereinafter "Therapeutics").

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An anti-FCTR_X antibody (*e.g.*, monoclonal antibody) can be used to isolate an FCTR_X polypeptide by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-FCTR_X antibody can facilitate the purification of natural FCTR_X polypeptide from cells and of recombinantly-produced FCTR_X polypeptide expressed in host cells. Moreover, an anti-FCTR_X antibody can be used to detect FCTR_X protein (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the FCTR_X protein. Anti-FCTR_X antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (*i.e.*, physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

FCTR_X Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an FCTR_X protein, or derivatives, fragments, analogs or homologs thereof. As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are

operatively-linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably-linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner that allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell).

The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Regulatory sequences include those that direct constitutive expression of a nucleotide sequence in many types of host cell and those that direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (*e.g.*, FCTR proteins, mutant forms of FCTR proteins, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of FCTR proteins in prokaryotic or eukaryotic cells. For example, FCTR proteins can be expressed in bacterial cells such as *Escherichia coli*, insect cells (using baculovirus expression vectors) yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990). Alternatively, the recombinant expression vector can be

transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: (i) to increase expression of recombinant protein; (ii) to increase the solubility of the recombinant protein; and (iii) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988. *Gene* 67: 31-40), pMAL (New England Biolabs, Beverly, Mass.) and pRIT5 (Pharmacia, Piscataway, N.J.) that fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amrann *et al.*, (1988) *Gene* 69:301-315) and pET 11d (Studier *et al.*, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 60-89).

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein. See, e.g., Gottesman, GENE EXPRESSION TECHNOLOGY: METHODS IN ENZYMOLOGY 185, Academic Press, San Diego, Calif. (1990) 119-128. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (see, e.g., Wada, *et al.*, 1992. *Nucl. Acids Res.* 20: 2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the FCTR_X expression vector is a yeast expression vector. Examples of vectors for expression in yeast *Saccharomyces cerevisiae* include pYepSec1 (Baldari, *et al.*, 1987. *EMBO J.* 6: 229-234), pMFa (Kurjan and Herskowitz, 1982. *Cell* 30: 933-943), pJRY88 (Schultz *et al.*, 1987. *Gene* 54: 113-123), pYES2 (Invitrogen Corporation, San Diego, Calif.), and picZ (Invitrogen Corp, San Diego, Calif.).

Alternatively, FCTR_X can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., SF9 cells) include the pAc series (Smith, *et al.*, 1983. *Mol. Cell. Biol.* 3: 2156-2165) and the pVL series (Lucklow and Summers, 1989. *Virology* 170: 31-39).

5 In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987. *Nature* 329: 840) and pMT2PC (Kaufman, *et al.*, 1987. *EMBO J.* 6: 187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used
10 promoters are derived from polyoma, adenovirus 2, cytomegalovirus, and simian virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see, e.g., Chapters 16 and 17 of Sambrook, *et al.*, MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989.

15 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert, *et al.*, 1987. *Genes Dev.* 1: 268-277), lymphoid-specific promoters (Calame and Eaton, 1988. *Adv. Immunol.* 43: 235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989. *EMBO J.* 8: 729-733) and immunoglobulins (Banerji, *et al.*, 1983. *Cell* 33: 729-740; Queen and Baltimore, 1983. *Cell* 33: 741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle, 1989. *Proc. Natl. Acad. Sci. USA* 86: 5473-5477),
20 pancreas-specific promoters (Edlund, *et al.*, 1985. *Science* 230: 912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Pat. No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, e.g., the murine hox promoters (Kessel and Gruss, 1990. *Science* 249: 374-379) and the α -fetoprotein promoter (Campes and Tilghman, 1989. *Genes Dev.* 3: 537-546).
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The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively-linked to a regulatory sequence in a manner that allows

for expression (by transcription of the DNA molecule) of an RNA molecule that is antisense to FCTR_X mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen that direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen that direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes *see, e.g.,* Weintraub, *et al.*, "Antisense RNA as a molecular tool for genetic analysis," *Reviews-Trends in Genetics*, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, FCTR_X protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.,* DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (MOLECULAR CLONING: A LABORATORY MANUAL. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene

that encodes a selectable marker (*e.g.*, resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Various selectable markers include those that confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding FCTR_X or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) FCTR_X protein. Accordingly, the invention further provides methods for producing FCTR_X protein using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding FCTR_X protein has been introduced) in a suitable medium such that FCTR_X protein is produced. In another embodiment, the method further comprises isolating FCTR_X protein from the medium or the host cell.

Transgenic FCTR_X Animals

The host cells of the invention can also be used to produce non-human transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which FCTR_X protein-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous FCTR_X sequences have been introduced into their genome or homologous recombinant animals in which endogenous FCTR_X sequences have been altered. Such animals are useful for studying the function and/or activity of FCTR_X protein and for identifying and/or evaluating modulators of FCTR_X protein activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA that is integrated into the genome of a cell from which a transgenic animal develops and that remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, a "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous FCTR_X gene has been altered by homologous recombination between the

endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing FCTR_X-encoding nucleic acid into the male pronuclei of a fertilized oocyte (*e.g.*, by microinjection, retroviral infection) and allowing the oocyte to develop in a pseudopregnant female foster animal. The human FCTR_X cDNA sequences of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be introduced as a transgene into the genome of a non-human animal.

Alternatively, a non-human homologue of the human FCTR_X gene, such as a mouse FCTR_X gene, can be isolated based on hybridization to the human FCTR_X cDNA (described further *supra*) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably-linked to the FCTR_X transgene to direct expression of FCTR_X protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866; 4,870,009; and 4,873,191; and Hogan, 1986. In: MANIPULATING THE MOUSE EMBRYO, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the FCTR_X transgene in its genome and/or expression of FCTR_X mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene-encoding FCTR_X protein can further be bred to other transgenic animals carrying other transgenes.

To create a homologous recombinant animal, a vector is prepared which contains at least a portion of an FCTR_X gene into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the FCTR_X gene. The FCTR_X gene can be a human gene (*e.g.*, the cDNA of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24), but more preferably, is a non-human homologue of a human FCTR_X gene. For example, a mouse homologue of human FCTR_X gene of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, can be used to construct a homologous recombination vector suitable for altering an endogenous FCTR_X gene in the mouse genome. In one embodiment, the vector is designed such that, upon homologous recombination, the endogenous FCTR_X gene is functionally disrupted (*i.e.*, no longer encodes a functional protein; also referred to as a "knock out" vector).

Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous FCTR_X gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby alter the expression of the endogenous FCTR_X protein). In the homologous recombination vector, the altered portion of the FCTR_X gene is flanked at its 5'- and 3'-termini by additional nucleic acid of the FCTR_X gene to allow for homologous recombination to occur between the exogenous FCTR_X gene carried by the vector and an endogenous FCTR_X gene in an embryonic stem cell. The additional flanking FCTR_X nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5'- and 3'-termini) are included in the vector. See, e.g., Thomas, *et al.*, 1987. *Cell* 51: 503 for a description of homologous recombination vectors. The vector is then introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced FCTR_X gene has homologously-recombined with the endogenous FCTR_X gene are selected. See, e.g., Li, *et al.*, 1992. *Cell* 69: 915.

The selected cells are then injected into a blastocyst of an animal (e.g., a mouse) to form aggregation chimeras. See, e.g., Bradley, 1987. In: TERATOCARCINOMAS AND EMBRYONIC STEM CELLS: A PRACTICAL APPROACH, Robertson, ed. IRL, Oxford, pp. 113-152. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously-recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously-recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley, 1991. *Curr. Opin. Biotechnol.* 2: 823-829; PCT International Publication Nos.: WO 90/11354; WO 91/01140; WO 92/0968; and WO 93/04169.

In another embodiment, transgenic non-humans animals can be produced that contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, See, e.g., Lakso, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae*. See, O'Gorman, *et al.*, 1991. *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g.,

by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, *et al.*, 1997. *Nature* 385: 810-813. In brief, a cell (*e.g.*, a somatic cell) from the transgenic animal can be isolated and induced to exit the growth cycle and enter G₀ phase. The quiescent cell can then be fused, *e.g.*, through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell (*e.g.*, the somatic cell) is isolated.

Pharmaceutical Compositions

The FCTR_X nucleic acid molecules, FCTR_X proteins, and anti-FCTR_X antibodies (also referred to herein as "active compounds") of the invention, and derivatives, fragments, analogs and homologs thereof, can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Suitable carriers are described in the most recent edition of Remington's Pharmaceutical Sciences, a standard reference text in the field, which is incorporated herein by reference. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, finger's solutions, dextrose solution, and 5% human serum albumin. Liposomes and non-aqueous vehicles such as fixed oils may also be used. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (*i.e.*, topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile

diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringeability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., an FCTR protein or anti-FCTR antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the

preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of

such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (*see, e.g.*, U.S. Patent No. 5,328,470) or by stereotactic injection (*see, e.g.*, Chen, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells that produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

Screening and Detection Methods

The isolated nucleic acid molecules of the invention can be used to express FCTR_X protein (*e.g.*, via a recombinant expression vector in a host cell in gene therapy applications), to detect FCTR_X mRNA (*e.g.*, in a biological sample) or a genetic lesion in an FCTR_X gene, and to modulate FCTR_X activity, as described further, below. In addition, the FCTR_X proteins can be used to screen drugs or compounds that modulate the FCTR_X protein activity or expression as well as to treat disorders characterized by insufficient or excessive

production of FCTR_X protein or production of FCTR_X protein forms that have decreased or aberrant activity compared to FCTR_X wild-type protein (*e.g.*; diabetes (regulates insulin release); obesity (binds and transport lipids); metabolic disturbances associated with obesity, the metabolic syndrome X as well as anorexia and wasting disorders associated with chronic diseases and various cancers, and infectious disease (possesses anti-microbial activity) and the various dyslipidemias. In addition, the anti-FCTR_X antibodies of the invention can be used to detect and isolate FCTR_X proteins and modulate FCTR_X activity. In yet a further aspect, the invention can be used in methods to influence appetite, absorption of nutrients and the disposition of metabolic substrates in both a positive and negative fashion.

The invention further pertains to novel agents identified by the screening assays described herein and uses thereof for treatments as described, *supra*.

Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, *i.e.*, candidate or test compounds or agents (*e.g.*, peptides, peptidomimetics, small molecules or other drugs) that bind to FCTR_X proteins or have a stimulatory or inhibitory effect on, *e.g.*, FCTR_X protein expression or FCTR_X protein activity. The invention also includes compounds identified in the screening assays described herein.

In one embodiment, the invention provides assays for screening candidate or test compounds which bind to or modulate the activity of the membrane-bound form of an FCTR_X protein or polypeptide or biologically-active portion thereof. The test compounds of the invention can be obtained using any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the "one-bead one-compound" library method; and synthetic library methods using affinity chromatography selection. The biological library approach is limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds. *See, e.g.*, Lam, 1997. *Anticancer Drug Design* 12: 145.

A "small molecule" as used herein, is meant to refer to a composition that has a molecular weight of less than about 5 kD and most preferably less than about 4 kD. Small molecules can be, *e.g.*, nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention.

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt, *et al.*, 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90: 6909; Erb, *et al.*, 1994. *Proc. Natl. Acad. Sci. U.S.A.* 91: 11422; Zuckermann, *et al.*, 1994. *J. Med. Chem.* 37: 2678; Cho, *et al.*, 1993. *Science* 261: 1303; Carrell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2059; Carell, *et al.*, 1994. *Angew. Chem. Int. Ed. Engl.* 33: 2061; and Gallop, *et al.*, 1994. *J. Med. Chem.* 37: 1233.

Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992. *Biotechniques* 13: 412-421), or on beads (Lam, 1991. *Nature* 354: 82-84), on chips (Fodor, 1993. *Nature* 364: 555-556), bacteria (Ladner, U.S. Patent No. 5,223,409), spores (Ladner, U.S. Patent 5,233,409), plasmids (Cull, *et al.*, 1992. *Proc. Natl. Acad. Sci. USA* 89: 1865-1869) or on phage (Scott and Smith, 1990. *Science* 249: 386-390; Devlin, 1990. *Science* 249: 404-406; Cwirla, *et al.*, 1990. *Proc. Natl. Acad. Sci. U.S.A.* 87: 6378-6382; Felici, 1991. *J. Mol. Biol.* 222: 301-310; Ladner, U.S. Patent No. 5,233,409.).

In one embodiment, an assay is a cell-based assay in which a cell which expresses a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface is contacted with a test compound and the ability of the test compound to bind to an FCTR_X protein determined. The cell, for example, can be of mammalian origin or a yeast cell. Determining the ability of the test compound to bind to the FCTR_X protein can be accomplished, for example, by coupling the test compound with a radioisotope or enzymatic label such that binding of the test compound to the FCTR_X protein or biologically-active portion thereof can be determined by detecting the labeled compound in a complex. For example, test compounds can be labeled with ¹²⁵I, ³⁵S, ¹⁴C, or ³H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, test compounds can be enzymatically-labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product. In one embodiment, the assay comprises contacting a cell which expresses a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface with a known compound which binds FCTR_X to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the test compound to preferentially bind to FCTR_X protein or a biologically-active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-based assay comprising contacting a cell expressing a membrane-bound form of FCTR_X protein, or a biologically-active portion thereof, on the cell surface with a test compound and determining the ability of the test compound to modulate (*e.g.*, stimulate or inhibit) the activity of the FCTR_X protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTR_X or a biologically-active portion thereof can be accomplished, for example, by determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule. As used herein, a "target molecule" is a molecule with which an FCTR_X protein binds or interacts in nature, for example, a molecule on the surface of a cell which expresses an FCTR_X interacting protein, a molecule on the surface of a second cell, a molecule in the extracellular milieu, a molecule associated with the internal surface of a cell membrane or a cytoplasmic molecule. An FCTR_X target molecule can be a non-FCTR_X molecule or an FCTR_X protein or polypeptide of the invention. In one embodiment, an FCTR_X target molecule is a component of a signal transduction pathway that facilitates transduction of an extracellular signal (*e.g.* a signal generated by binding of a compound to a membrane-bound FCTR_X molecule) through the cell membrane and into the cell. The target, for example, can be a second intercellular protein that has catalytic activity or a protein that facilitates the association of downstream signaling molecules with FCTR_X.

Determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule can be accomplished by one of the methods described above for determining direct binding. In one embodiment, determining the ability of the FCTR_X protein to bind to or interact with an FCTR_X target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the target (*i.e.* intracellular Ca²⁺, diacylglycerol, IP₃, etc.), detecting catalytic/enzymatic activity of the target an appropriate substrate, detecting the induction of a reporter gene (comprising an FCTR_X-responsive regulatory element operatively linked to a nucleic acid encoding a detectable marker, *e.g.*, luciferase), or detecting a cellular response, for example, cell survival, cellular differentiation, or cell proliferation.

In yet another embodiment, an assay of the invention is a cell-free assay comprising contacting an FCTR_X protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to bind to the FCTR_X protein or biologically-active portion thereof. Binding of the test compound to the FCTR_X protein can be determined either directly or indirectly as described above. In one such embodiment, the

assay comprises contacting the FCTR_X protein or biologically-active portion thereof with a known compound which binds FCTR_X to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the test compound to preferentially bind to FCTR_X or biologically-active portion thereof as compared to the known compound.

In still another embodiment, an assay is a cell-free assay comprising contacting FCTR_X protein or biologically-active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g. stimulate or inhibit) the activity of the FCTR_X protein or biologically-active portion thereof. Determining the ability of the test compound to modulate the activity of FCTR_X can be accomplished, for example, by determining the ability of the FCTR_X protein to bind to an FCTR_X target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of FCTR_X protein can be accomplished by determining the ability of the FCTR_X protein further modulate an FCTR_X target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as described, *supra*.

In yet another embodiment, the cell-free assay comprises contacting the FCTR_X protein or biologically-active portion thereof with a known compound which binds FCTR_X protein to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with an FCTR_X protein, wherein determining the ability of the test compound to interact with an FCTR_X protein comprises determining the ability of the FCTR_X protein to preferentially bind to or modulate the activity of an FCTR_X target molecule.

The cell-free assays of the invention are amenable to use of both the soluble form or the membrane-bound form of FCTR_X protein. In the case of cell-free assays comprising the membrane-bound form of FCTR_X protein, it may be desirable to utilize a solubilizing agent such that the membrane-bound form of FCTR_X protein is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide, Triton[®] X-100, Triton[®] X-114, Thesit[®], Isotridecypoly(ethylene glycol ether)_n, N-dodecyl--N,N-dimethyl-3-ammonio-1-propane sulfonate, 3-(3-cholamidopropyl) dimethylamminiol-1-propane sulfonate (CHAPS), or 3-(3-cholamidopropyl)dimethylamminiol-2-hydroxy-1-propane sulfonate (CHAPSO).

In more than one embodiment of the above assay methods of the invention, it may be desirable to immobilize either FCTR_X protein or its target molecule to facilitate separation of complexed from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to FCTR_X protein, or interaction of FCTR_X protein with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtiter plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided that adds a domain that allows one or both of the proteins to be bound to a matrix. For example, GST-FCTR_X fusion proteins or GST-target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, that are then combined with the test compound or the test compound and either the non-adsorbed target protein or FCTR_X protein, and the mixture is incubated under conditions conducive to complex formation (*e.g.*, at physiological conditions for salt and pH). Following incubation, the beads or microtiter plate wells are washed to remove any unbound components, the matrix immobilized in the case of beads, complex determined either directly or indirectly, for example, as described, *supra*. Alternatively, the complexes can be dissociated from the matrix, and the level of FCTR_X protein binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either the FCTR_X protein or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated FCTR_X protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well-known within the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, Ill.), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with FCTR_X protein or target molecules, but which do not interfere with binding of the FCTR_X protein to its target molecule, can be derivatized to the wells of the plate, and unbound target or FCTR_X protein trapped in the wells by antibody conjugation. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the FCTR_X protein or target molecule, as well as enzyme-linked assays that rely on detecting an enzymatic activity associated with the FCTR_X protein or target molecule.

In another embodiment, modulators of FCTR_X protein expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of FCTR_X

mRNA or protein in the cell is determined. The level of expression of FCTR_X mRNA or protein in the presence of the candidate compound is compared to the level of expression of FCTR_X mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of FCTR_X mRNA or protein expression based upon this comparison. For example, when expression of FCTR_X mRNA or protein is greater (*i.e.*, statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of FCTR_X mRNA or protein expression. Alternatively, when expression of FCTR_X mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of FCTR_X mRNA or protein expression. The level of FCTR_X mRNA or protein expression in the cells can be determined by methods described herein for detecting FCTR_X mRNA or protein.

In yet another aspect of the invention, the FCTR_X proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (*see, e.g.*, U.S. Patent No. 5,283,317; Zervos, *et al.*, 1993. *Cell* 72: 223-232; Madura, *et al.*, 1993. *J. Biol. Chem.* 268: 12046-12054; Bartel, *et al.*, 1993. *Biotechniques* 14: 920-924; Iwabuchi, *et al.*, 1993. *Oncogene* 8: 1693-1696; and Brent WO 94/10300), to identify other proteins that bind to or interact with FCTR_X ("FCTR_X-binding proteins" or "FCTR_X-bp") and modulate FCTR_X activity. Such FCTR_X-binding proteins are also likely to be involved in the propagation of signals by the FCTR_X proteins as, for example, upstream or downstream elements of the FCTR_X pathway.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for FCTR_X is fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.*, GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an FCTR_X-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.*, LacZ) that is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene that encodes the protein which interacts with FCTR_X.

The invention further pertains to novel agents identified by the aforementioned screening assays and uses thereof for treatments as described herein.

Detection Assays

Portions or fragments of the cDNA sequences identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. By way of example, and not of limitation, these sequences can be used to: (i) map their respective genes on a chromosome; and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. Some of these applications are described in the subsections, below.

Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. This process is called chromosome mapping. Accordingly, portions or fragments of the FCTR_X sequences, SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or fragments or derivatives thereof, can be used to map the location of the FCTR_X genes, respectively, on a chromosome. The mapping of the FCTR_X sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, FCTR_X genes can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the FCTR_X sequences. Computer analysis of the FCTR_X sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the FCTR_X sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow, because they lack a particular enzyme, but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy

mapping of individual genes to specific human chromosomes. *See, e.g., D'Eustachio, et al., 1983. Science 220: 919-924.* Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

5 PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the FCTR_X sequences to design oligonucleotide primers, sub-localization can be achieved with panels of fragments from specific chromosomes.

10 Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical like colcemid that disrupts the mitotic spindle. The chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark
15 bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases, will suffice to get good results at a reasonable
20 amount of time. For a review of this technique, *see, Verma, et al., HUMAN CHROMOSOMES: A MANUAL OF BASIC TECHNIQUES* (Pergamon Press, New York 1988).

 Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding
25 regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

 Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such
30 data are found, *e.g., in McKusick, MENDELIAN INHERITANCE IN MAN*, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, *e.g., Egeland, et al., 1987. Nature, 325: 783-787.*

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease associated with the FCTR_X gene, can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes, such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

Tissue Typing

The FCTR_X sequences of the invention can also be used to identify individuals from minute biological samples. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. The sequences of the invention are useful as additional DNA markers for RFLP ("restriction fragment length polymorphisms," described in U.S. Patent No. 5,272,057).

Furthermore, the sequences of the invention can be used to provide an alternative technique that determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the FCTR_X sequences described herein can be used to prepare two PCR primers from the 5'- and 3'-termini of the sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the invention can be used to obtain such identification sequences from individuals and from tissue. The FCTR_X sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Much of the allelic variation is due to single nucleotide polymorphisms (SNPs), which include restriction fragment length polymorphisms (RFLPs).

Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are

necessary to differentiate individuals. The noncoding sequences can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers that each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

Predictive Medicine

The invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trials are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the invention relates to diagnostic assays for determining FCTR_X protein and/or nucleic acid expression as well as FCTR_X activity, in the context of a biological sample (*e.g.*, blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant FCTR_X expression or activity. The disorders include Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal

dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with FCTR_X protein, nucleic acid expression or activity. For example, mutations in an FCTR_X gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with FCTR_X protein, nucleic acid expression, or biological activity.

Another aspect of the invention provides methods for determining FCTR_X protein, nucleic acid expression or activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of FCTR_X in clinical trials.

These and other agents are described in further detail in the following sections.

Diagnostic Assays

An exemplary method for detecting the presence or absence of FCTR_X in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting FCTR_X protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes FCTR_X protein such that the presence of FCTR_X is detected in the biological sample. An agent for detecting FCTR_X mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to FCTR_X mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length FCTR_X nucleic acid, such as the nucleic acid of SEQ ID NOS:1, 3, 5, 7, 9, 10, 11, 12, 14, 16, 18, 20, 22, and 24, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to FCTR_X mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

An agent for detecting FCTR_X protein is an antibody capable of binding to FCTR_X protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) can be used. The term "labeled", with regard to the probe or antibody, is intended to

encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently-labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently-labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect FCTR_X mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*.

For example, *in vitro* techniques for detection of FCTR_X mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of FCTR_X protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations, and immunofluorescence. *In vitro* techniques for detection of FCTR_X genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of FCTR_X protein include introducing into a subject a labeled anti-FCTR_X antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting FCTR_X protein, mRNA, or genomic DNA, such that the presence of FCTR_X protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of FCTR_X protein, mRNA or genomic DNA in the control sample with the presence of FCTR_X protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of FCTR_X in a biological sample. For example, the kit can comprise: a labeled compound or agent capable of detecting FCTR_X protein or mRNA in a biological sample; means for determining the amount of FCTR_X in the sample; and means for comparing the amount of FCTR_X in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect FCTR_X protein or nucleic acid.

Prognostic Assays

The diagnostic methods described herein can furthermore be utilized to identify subjects having or at risk of developing a disease or disorder associated with aberrant FCTR_X expression or activity. For example, the assays described herein, such as the preceding

5 diagnostic assays or the following assays, can be utilized to identify a subject having or at risk of developing a disorder associated with FCTR_X protein, nucleic acid expression or activity. Alternatively, the prognostic assays can be utilized to identify a subject having or at risk for developing a disease or disorder. Thus, the invention provides a method for identifying a disease or disorder associated with aberrant FCTR_X expression or activity in

10 which a test sample is obtained from a subject and FCTR_X protein or nucleic acid (*e.g.*, mRNA, genomic DNA) is detected, wherein the presence of FCTR_X protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant FCTR_X expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological

15 fluid (*e.g.*, serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant FCTR_X expression or activity. For example, such methods can be

20 used to determine whether a subject can be effectively treated with an agent for a disorder. Thus, the invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant FCTR_X expression or activity in which a test sample is obtained and FCTR_X protein or nucleic acid is detected (*e.g.*, wherein the presence of FCTR_X protein or nucleic acid is diagnostic for a subject that can be

25 administered the agent to treat a disorder associated with aberrant FCTR_X expression or activity).

The methods of the invention can also be used to detect genetic lesions in an FCTR_X gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant cell proliferation and/or differentiation. In various embodiments,

30 the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion characterized by at least one of an alteration affecting the integrity of a gene encoding an FCTR_X-protein, or the misexpression of the FCTR_X gene. For example, such genetic lesions can be detected by ascertaining the existence of at least one of: (i) a deletion of one or more nucleotides from an FCTR_X gene; (ii) an addition of one or more

nucleotides to an FCTR_X gene; (iii) a substitution of one or more nucleotides of an FCTR_X gene, (iv) a chromosomal rearrangement of an FCTR_X gene; (v) an alteration in the level of a messenger RNA transcript of an FCTR_X gene, (vi) aberrant modification of an FCTR_X gene, such as of the methylation pattern of the genomic DNA, (vii) the presence of a non-wild-type splicing pattern of a messenger RNA transcript of an FCTR_X gene, (viii) a non-wild-type level of an FCTR_X protein, (ix) allelic loss of an FCTR_X gene, and (x) inappropriate post-translational modification of an FCTR_X protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions in an FCTR_X gene. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.*, U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.*, Landegran, *et al.*, 1988. *Science* 241: 1077-1080; and Nakazawa, *et al.*, 1994. *Proc. Natl. Acad. Sci. USA* 91: 360-364), the latter of which can be particularly useful for detecting point mutations in the FCTR_X-gene (*see*, Abravaya, *et al.*, 1995. *Nucl. Acids Res.* 23: 675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers that specifically hybridize to an FCTR_X gene under conditions such that hybridization and amplification of the FCTR_X gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (*see*, Guatelli, *et al.*, 1990. *Proc. Natl. Acad. Sci. USA* 87: 1874-1878), transcriptional amplification system (*see*, Kwoh, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA* 86: 1173-1177); Q β Replicase (*see*, Lizardi, *et al.*, 1988. *BioTechnology* 6: 1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

1 In an alternative embodiment, mutations in an FCTR_X gene from a sample cell can be
identified by alterations in restriction enzyme cleavage patterns. For example, sample and
control DNA is isolated, amplified (optionally), digested with one or more restriction
endonucleases, and fragment length sizes are determined by gel electrophoresis and
5 compared. Differences in fragment length sizes between sample and control DNA indicates
mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (*see, e.g.*,
U.S. Patent No. 5,493,531) can be used to score for the presence of specific mutations by
development or loss of a ribozyme cleavage site.

10 In other embodiments, genetic mutations in FCTR_X can be identified by hybridizing a
sample and control nucleic acids, *e.g.*, DNA or RNA, to high-density arrays containing
hundreds or thousands of oligonucleotides probes. *See, e.g.*, Cronin, *et al.*, 1996. *Human*
Mutation 7: 244-255; Kozal, *et al.*, 1996. *Nat. Med.* 2: 753-759. For example, genetic
mutations in FCTR_X can be identified in two dimensional arrays containing light-generated
15 DNA probes as described in Cronin, *et al.*, *supra*. Briefly, a first hybridization array of
probes can be used to scan through long stretches of DNA in a sample and control to identify
base changes between the sequences by making linear arrays of sequential overlapping
probes. This step allows the identification of point mutations. This is followed by a second
hybridization array that allows the characterization of specific mutations by using smaller,
specialized probe arrays complementary to all variants or mutations detected. Each mutation
20 array is composed of parallel probe sets, one complementary to the wild-type gene and the
other complementary to the mutant gene.

25 In yet another embodiment, any of a variety of sequencing reactions known in the art
can be used to directly sequence the FCTR_X gene and detect mutations by comparing the
sequence of the sample FCTR_X with the corresponding wild-type (control) sequence.
Examples of sequencing reactions include those based on techniques developed by Maxim
and Gilbert, 1977. *Proc. Natl. Acad. Sci. USA* 74: 560 or Sanger, 1977. *Proc. Natl. Acad. Sci.*
USA 74: 5463. It is also contemplated that any of a variety of automated sequencing
procedures can be utilized when performing the diagnostic assays (*see, e.g.*, Naeve, *et al.*,
1995. *Biotechniques* 19: 448), including sequencing by mass spectrometry (*see, e.g.*, PCT
30 International Publication No. WO 94/16101; Cohen, *et al.*, 1996. *Adv. Chromatography* 36:
127-162; and Griffin, *et al.*, 1993. *Appl. Biochem. Biotechnol.* 38: 147-159).

Other methods for detecting mutations in the FCTR_X gene include methods in which
protection from cleavage agents is used to detect mismatched bases in RNA/RNA or
RNA/DNA heteroduplexes. *See, e.g.*, Myers, *et al.*, 1985. *Science* 230: 1242. In general, the

art technique of "mismatch cleavage" starts by providing heteroduplexes of formed by hybridizing (labeled) RNA or DNA containing the wild-type FCTR_X sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent that cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and sample strands. For instance, RNA/DNA duplexes can be treated with RNase and DNA/DNA hybrids treated with S₁ nuclease to enzymatically digesting the mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton, *et al.*, 1988. *Proc. Natl. Acad. Sci. USA* 85: 4397; Saleeba, *et al.*, 1992. *Methods Enzymol.* 217: 286-295. In an embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize mismatched base pairs in double-stranded DNA (so called "DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in FCTR_X cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches. See, e.g., Hsu, *et al.*, 1994. *Carcinogenesis* 15: 1657-1662. According to an exemplary embodiment, a probe based on an FCTR_X sequence, e.g., a wild-type FCTR_X sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in FCTR_X genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids. See, e.g., Orita, *et al.*, 1989. *Proc. Natl. Acad. Sci. USA*: 86: 2766; Cotton, 1993. *Mutat. Res.* 285: 125-144; Hayashi, 1992. *Genet. Anal. Tech. Appl.* 9: 73-79.

Single-stranded DNA fragments of sample and control FCTR_X nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In one

embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in electrophoretic mobility. *See, e.g., Keen, et al., 1991. Trends Genet. 7: 5.*

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE). *See, e.g., Myers, et al., 1985. Nature 313: 495.* When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA. *See, e.g., Rosenbaum and Reissner, 1987. Biophys. Chem. 265: 12753.*

Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the known mutation is placed centrally and then hybridized to target DNA under conditions that permit hybridization only if a perfect match is found. *See, e.g., Saiki, et al., 1986. Nature 324: 163; Saiki, et al., 1989. Proc. Natl. Acad. Sci. USA 86: 6230.* Such allele specific oligonucleotides are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification technology that depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on differential hybridization; *see, e.g., Gibbs, et al., 1989. Nucl. Acids Res. 17: 2437-2448*) or at the extreme 3'-terminus of one primer where, under appropriate conditions, mismatch can prevent, or reduce polymerase extension (*see, e.g., Prossner, 1993. Tibtech. 11: 238*). In addition it may be desirable to introduce a novel restriction site in the region of the mutation to create cleavage-based detection. *See, e.g., Gasparini, et al., 1992. Mol. Cell Probes 6: 1.* It is anticipated that in certain embodiments amplification may also be performed using *Taq* ligase for amplification. *See, e.g., Barany, 1991. Proc. Natl. Acad. Sci. USA 88: 189.* In such cases, ligation will occur only if there is a perfect match at the 3'-terminus of the 5' sequence, making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, *e.g.*, in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving an FCTR_X gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which FCTR_X is expressed may be utilized in the prognostic assays described herein. However, any biological sample containing nucleated cells may be used, including, for example, buccal mucosal cells.

Pharmacogenomics

Agents, or modulators that have a stimulatory or inhibitory effect on FCTR_X activity (*e.g.*, FCTR_X gene expression), as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (The disorders include metabolic disorders, Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital ceonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma , clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, *Schistosoma mansoni* infection, Spinocerebellar ataxia, *Plasmodium falciparum* parasitemia, Corneal dystrophy -

Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy) In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of FCTR protein, expression of FCTR nucleic acid, or mutation content of FCTR genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See *e.g.*, Eichelbaum, 1996. *Clin. Exp. Pharmacol. Physiol.*, 23: 983-985; Linder, 1997. *Clin. Chem.*, 43: 254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way the body acts on drugs (altered drug metabolism). These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug

response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. At the other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses.

5 Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of FCTR_X protein, expression of FCTR_X nucleic acid, or mutation content of FCTR_X genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition,

10 pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with an FCTR_X modulator, such as a modulator identified by one of the
15 exemplary screening assays described herein.

Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (*e.g.*, drugs, compounds) on the expression or activity of FCTR_X (*e.g.*, the ability to modulate aberrant cell proliferation and/or differentiation) can be applied not only in basic drug screening, but also in clinical trials. For
20 example, the effectiveness of an agent determined by a screening assay as described herein to increase FCTR_X gene expression, protein levels, or upregulate FCTR_X activity, can be monitored in clinical trails of subjects exhibiting decreased FCTR_X gene expression, protein levels, or downregulated FCTR_X activity. Alternatively, the effectiveness of an agent determined by a screening assay to decrease FCTR_X gene expression, protein levels, or
25 downregulate FCTR_X activity, can be monitored in clinical trails of subjects exhibiting increased FCTR_X gene expression, protein levels, or upregulated FCTR_X activity. In such clinical trials, the expression or activity of FCTR_X and, preferably, other genes that have been implicated in, for example, a cellular proliferation or immune disorder can be used as a "read out" or markers of the immune responsiveness of a particular cell.

30 By way of example, and not of limitation, genes, including FCTR_X, that are modulated in cells by treatment with an agent (*e.g.*, compound, drug or small molecule) that modulates FCTR_X activity (*e.g.*, identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of

expression of FCTR_X and other genes implicated in the disorder. The levels of gene expression (*i.e.*, a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of FCTR_X or other genes. In this manner, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In one embodiment, the invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, protein, peptide, peptidomimetic, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of an FCTR_X protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the FCTR_X protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the FCTR_X protein, mRNA, or genomic DNA in the pre-administration sample with the FCTR_X protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of FCTR_X to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of FCTR_X to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

Methods of Treatment

The invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disorder or having a disorder associated with aberrant FCTR_X expression or activity. The disorders include cardiomyopathy, atherosclerosis, hypertension, congenital heart defects, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, pulmonary stenosis, subaortic stenosis, ventricular septal defect (VSD), valve diseases, tuberous sclerosis, scleroderma, obesity, transplantation, adrenoleukodystrophy, congenital adrenal hyperplasia, prostate cancer, neoplasm; adenocarcinoma, lymphoma, uterus cancer, fertility, hemophilia, hypercoagulation, idiopathic thrombocytopenic purpura, immunodeficiencies, graft versus

host disease, AIDS, bronchial asthma, Crohn's disease; multiple sclerosis, treatment of Albright Hereditary Osteodystrophy, and other diseases, disorders and conditions of the like.

These methods of treatment will be discussed more fully, below.

Disease and Disorders

5 Diseases and disorders that are characterized by increased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that antagonize (*i.e.*, reduce or inhibit) activity. Therapeutics that antagonize activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to: (i) an aforementioned peptide, or analogs,
10 derivatives, fragments or homologs thereof; (ii) antibodies to an aforementioned peptide; (iii) nucleic acids encoding an aforementioned peptide; (iv) administration of antisense nucleic acid and nucleic acids that are "dysfunctional" (*i.e.*, due to a heterologous insertion within the coding sequences of coding sequences to an aforementioned peptide) that are utilized to "knockout" endogenous function of an aforementioned peptide by homologous
15 recombination (*see, e.g.*, Capecchi, 1989. *Science* 244: 1288-1292); or (v) modulators (*i.e.*, inhibitors, agonists and antagonists, including additional peptide mimetic of the invention or antibodies specific to a peptide of the invention) that alter the interaction between an aforementioned peptide and its binding partner.

20 Diseases and disorders that are characterized by decreased (relative to a subject not suffering from the disease or disorder) levels or biological activity may be treated with Therapeutics that increase (*i.e.*, are agonists to) activity. Therapeutics that upregulate activity may be administered in a therapeutic or prophylactic manner. Therapeutics that may be utilized include, but are not limited to, an aforementioned peptide, or analogs, derivatives, fragments or homologs thereof; or an agonist that increases bioavailability.

25 Increased or decreased levels can be readily detected by quantifying peptide and/or RNA, by obtaining a patient tissue sample (*e.g.*, from biopsy tissue) and assaying it *in vitro* for RNA or peptide levels, structure and/or activity of the expressed peptides (or mRNAs of an aforementioned peptide). Methods that are well-known within the art include, but are not limited to, immunoassays (*e.g.*, by Western blot analysis, immunoprecipitation followed by
30 sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis, immunocytochemistry, etc.) and/or hybridization assays to detect expression of mRNAs (*e.g.*, Northern assays, dot blots, *in situ* hybridization, and the like).

Prophylactic Methods

In one aspect, the invention provides a method for preventing, in a subject, a disease or condition associated with an aberrant FCTR_X expression or activity, by administering to the subject an agent that modulates FCTR_X expression or at least one FCTR_X activity.

5 Subjects at risk for a disease that is caused or contributed to by aberrant FCTR_X expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the FCTR_X aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending upon the type
10 of FCTR_X aberrancy, for example, an FCTR_X agonist or FCTR_X antagonist agent can be used for treating the subject. The appropriate agent can be determined based on screening assays described herein. The prophylactic methods of the invention are further discussed in the following subsections.

Therapeutic Methods

15 Another aspect of the invention pertains to methods of modulating FCTR_X expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of FCTR_X protein activity associated with the cell. An agent that modulates FCTR_X protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate
20 ligand of an FCTR_X protein, a peptide, an FCTR_X peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more FCTR_X protein activity. Examples of such stimulatory agents include active FCTR_X protein and a nucleic acid molecule encoding FCTR_X that has been introduced into the cell. In another embodiment, the agent inhibits one or more FCTR_X protein activity. Examples of such inhibitory agents include antisense
25 FCTR_X nucleic acid molecules and anti-FCTR_X antibodies. These modulatory methods can be performed *in vitro* (e.g., by culturing the cell with the agent) or, alternatively, *in vivo* (e.g., by administering the agent to a subject). As such, the invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of an FCTR_X protein or nucleic acid molecule. In one embodiment, the method
30 involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., up-regulates or down-regulates) FCTR_X expression or activity. In another embodiment, the method involves administering an FCTR_X protein or nucleic acid molecule as therapy to compensate for reduced or aberrant FCTR_X expression or activity.

Stimulation of FCTR_X activity is desirable in situations in which FCTR_X is abnormally downregulated and/or in which increased FCTR_X activity is likely to have a beneficial effect. One example of such a situation is where a subject has a disorder characterized by aberrant cell proliferation and/or differentiation (*e.g.*, cancer or immune associated disorders). Another example of such a situation is where the subject has a gestational disease (*e.g.*, preeclampsia).

Determination of the Biological Effect of the Therapeutic

In various embodiments of the invention, suitable *in vitro* or *in vivo* assays are performed to determine the effect of a specific Therapeutic and whether its administration is indicated for treatment of the affected tissue.

In various specific embodiments, *in vitro* assays may be performed with representative cells of the type(s) involved in the patient's disorder, to determine if a given Therapeutic exerts the desired effect upon the cell type(s). Compounds for use in therapy may be tested in suitable animal model systems including, but not limited to rats, mice, chicken, cows, monkeys, rabbits, and the like, prior to testing in human subjects. Similarly, for *in vivo* testing, any of the animal model system known in the art may be used prior to administration to human subjects.

Prophylactic and Therapeutic Uses of the Compositions of the Invention

The FCTR_X nucleic acids and proteins of the invention are useful in potential prophylactic and therapeutic applications implicated in a variety of disorders including, but not limited to: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paranechmal and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune

surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy -Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

As an example, a cDNA encoding the FCTR protein of the invention may be useful in gene therapy, and the protein may be useful when administered to a subject in need thereof. By way of non-limiting example, the compositions of the invention will have efficacy for treatment of patients suffering from: Also within the scope of the invention is the use of a Therapeutic in the manufacture of a medicament for treating or preventing disorders or syndromes including, *e.g.*, Colorectal cancer, adenomatous polyposis coli, myelogenous leukemia, congenital neonatal alloimmune thrombocytopenia, multiple human solid malignancies, malignant ovarian tumours particularly at the interface between epithelia and stroma, malignant brain tumors, mammary tumors, human gliomas, astrocytomas, mixed glioma/astrocytomas, renal cells carcinoma, breast adenocarcinoma, ovarian cancer, melanomas, renal cell carcinoma, clear cell and granular cell carcinomas, autocrine/paracrine stimulation of tumor cell proliferation, autocrine/paracrine stimulation of tumor cell survival and tumor cell resistance to cytotoxic therapy, paraneoplastic and basement membrane invasion and motility of tumor cells thereby contributing to metastasis, tumor-mediated immunosuppression of T-cell mediated immune effector cells and pathways resulting in tumor escape from immune surveillance, neurological disorders, neurodegenerative disorders, nerve trauma, familial myelodysplastic syndrome, Charcot-Marie-Tooth neuropathy, demyelinating Gardner syndrome, familial myelodysplastic syndrome; mental health conditions, immunological disorders, allergy and infection, asthma, bronchial asthma, Avellino type eosinophilia, lung diseases, reproductive disorders, male infertility, female reproductive system disorders, male and female reproductive diseases, hemangioma, deafness, glycoprotein Ia deficiency, desmoid disease, turcot syndrome, liver cirrhosis, hepatitis C, gastric disorders, pancreatic diseases like diabetes, Schistosoma mansoni

infection, Spinocerebellar ataxia, Plasmodium falciparum parasitemia, Corneal dystrophy - Groenouw type I, Corneal dystrophy - lattice type I, and Reis-Bucklers corneal dystrophy.

Both the novel nucleic acid encoding the FCTR_X protein, and the FCTR_X protein of the invention, or fragments thereof, may also be useful in diagnostic applications, wherein the presence or amount of the nucleic acid or the protein are to be assessed. A further use could be as an anti-bacterial molecule (*i.e.*, some peptides have been found to possess anti-bacterial properties). These materials are further useful in the generation of antibodies which immunospecifically-bind to the novel substances of the invention for use in therapeutic or diagnostic methods.

EXAMPLES

The following examples illustrate by way of non-limiting example various aspects of the invention.

The following examples illustrate by way of non-limiting example various aspects of the invention.

Example 1: Method of Identifying the Nucleic Acids

The novel nucleic acids of the invention were identified by TblastN using a proprietary sequence file, run against the Genomic Daily Files made available by GenBank. The nucleic acids were further predicted by the proprietary software program GenScan™, including selection of exons. These were further modified by means of similarities using BLAST searches. The sequences were then manually corrected for apparent inconsistencies, thereby obtaining the sequences encoding the full-length proteins.

Example 2. Quantitative expression analysis of FCTR₂ in various cells and tissues

The quantitative expression of various clones was assessed using microtiter plates containing RNA samples from a variety of normal and pathology-derived cells, cell lines and tissues using real time quantitative PCR (RTQ PCR; TAQMAN®). RTQ PCR was performed on a Perkin-Elmer Biosystems ABI PRISM® 7700 Sequence Detection System. Various collections of samples are assembled on the plates, and referred to as Panel 1 (containing cells and cell lines from normal and cancer sources), Panel 2 (containing samples derived from tissues, in particular from surgical samples, from normal and cancer sources), Panel 3 (containing samples derived from a wide variety of cancer sources) and Panel 4

(containing cells and cell lines from normal cells and cells related to inflammatory conditions).

First, the RNA samples were normalized to constitutively expressed genes such as β -actin and GAPDH. RNA (~50 ng total or ~1 ng polyA+) was converted to cDNA using the TAQMAN® Reverse Transcription Reagents Kit (PE Biosystems, Foster City, CA; Catalog No. N808-0234) and random hexamers according to the manufacturer's protocol. Reactions were performed in 20 μ l and incubated for 30 min. at 48°C. cDNA (5 μ l) was then transferred to a separate plate for the TAQMAN® reaction using β -actin and GAPDH TAQMAN® Assay Reagents (PE Biosystems; Catalog Nos. 4310881E and 4310884E, respectively) and TAQMAN® universal PCR Master Mix (PE Biosystems; Catalog No. 4304447) according to the manufacturer's protocol. Reactions were performed in 25 μ l using the following parameters: 2 min. at 50°C; 10 min. at 95°C; 15 sec. at 95°C/1 min. at 60°C (40 cycles). Results were recorded as CT values (cycle at which a given sample crosses a threshold level of fluorescence) using a log scale, with the difference in RNA concentration between a given sample and the sample with the lowest CT value being represented as 2 to the power of delta CT. The percent relative expression is then obtained by taking the reciprocal of this RNA difference and multiplying by 100. The average CT values obtained for β -actin and GAPDH were used to normalize RNA samples. The RNA sample generating the highest CT value required no further diluting, while all other samples were diluted relative to this sample according to their β -actin /GAPDH average CT values.

Normalized RNA (5 μ l) was converted to cDNA and analyzed via TAQMAN® using One Step RT-PCR Master Mix Reagents (PE Biosystems; Catalog No. 4309169) and gene-specific primers according to the manufacturer's instructions. Probes and primers were designed for each assay according to Perkin Elmer Biosystem's *Primer Express* Software package (version I for Apple Computer's Macintosh Power PC) or a similar algorithm using the target sequence as input. Default settings were used for reaction conditions and the following parameters were set before selecting primers: primer concentration = 250 nM, primer melting temperature (T_m) range = 58°-60° C, primer optimal T_m = 59° C, maximum primer difference = 2° C, probe does not have 5' G, probe T_m must be 10° C greater than primer T_m , amplicon size 75 bp to 100 bp. The probes and primers selected (see below) were synthesized by Synthegen (Houston, TX, USA). Probes were double purified by HPLC to remove uncoupled dye and evaluated by mass spectroscopy to verify coupling of reporter and

quencher dyes to the 5' and 3' ends of the probe, respectively. Their final concentrations were: forward and reverse primers, 900 nM each, and probe, 200nM.

PCR conditions: Normalized RNA from each tissue and each cell line was spotted in each well of a 96 well PCR plate (Perkin Elmer Biosystems). PCR cocktails including two probes (a probe specific for the target clone and another gene-specific probe multiplexed with the target probe) were set up using 1X TaqMan™ PCR Master Mix for the PE Biosystems 7700, with 5 mM MgCl₂, dNTPs (dA, G, C, U at 1:1:1:2 ratios), 0.25 U/ml AmpliTaq Gold™ (PE Biosystems), and 0.4 U/μl RNase inhibitor, and 0.25 U/μl reverse transcriptase. Reverse transcription was performed at 48° C for 30 minutes followed by amplification/PCR cycles as follows: 95° C 10 min, then 40 cycles of 95° C for 15 seconds, 60° C for 1 minute.

In the results for Panel 1, the following abbreviations are used:

ca. = carcinoma,

* = established from metastasis,

met = metastasis,

s cell var= small cell variant,

non-s = non-sm =non-small,

squam = squamous,

pl. eff = pl effusion = pleural effusion,

glio = glioma,

astro = astrocytoma, and

neuro = neuroblastoma.

Panel 2

The plates for Panel 2 generally include 2 control wells and 94 test samples composed of RNA or cDNA isolated from human tissue procured by surgeons working in close cooperation with the National Cancer Institute's Cooperative Human Tissue Network (CHTN) or the National Disease Research Initiative (NDRI). The tissues are derived from human malignancies and in cases where indicated many malignant tissues have "matched margins" obtained from noncancerous tissue just adjacent to the tumor. These are termed normal adjacent tissues and are denoted "NAT" in the results below. The tumor tissue and the "matched margins" are evaluated by two independent pathologists (the surgical

pathologists and again by a pathologists at NDRI or CHTN). This analysis provides a gross histopathological assessment of tumor differentiation grade. Moreover, most samples include the original surgical pathology report that provides information regarding the clinical stage of the patient. These matched margins are taken from the tissue surrounding (i.e. immediately proximal) to the zone of surgery (designated "NAT", for normal adjacent tissue, in Table RR). In addition, RNA and cDNA samples were obtained from various human tissues derived from autopsies performed on elderly people or sudden death victims (accidents, etc.). These tissue were ascertained to be free of disease and were purchased from various commercial sources such as Clontech (Palo Alto, CA), Research Genetics, and Invitrogen.

RNA integrity from all samples is controlled for quality by visual assessment of agarose gel electropherograms using 28S and 18S ribosomal RNA staining intensity ratio as a guide (2:1 to 2.5:1 28s:18s) and the absence of low molecular weight RNAs that would be indicative of degradation products. Samples are controlled against genomic DNA contamination by RTQ PCR reactions run in the absence of reverse transcriptase using probe and primer sets designed to amplify across the span of a single exon.

Panel 4

Panel 4 includes samples on a 96 well plate (2 control wells, 94 test samples) composed of RNA (Panel 4r) or cDNA (Panel 4d) isolated from various human cell lines or tissues related to inflammatory conditions. Total RNA from control normal tissues such as colon and lung (Stratagene ,La Jolla, CA) and thymus and kidney (Clontech) were employed. Total RNA from liver tissue from cirrhosis patients and kidney from lupus patients was obtained from BioChain (Biochain Institute, Inc., Hayward, CA). Intestinal tissue for RNA preparation from patients diagnosed as having Crohn's disease and ulcerative colitis was obtained from the National Disease Research Interchange (NDRI) (Philadelphia, PA).

Astrocytes, lung fibroblasts, dermal fibroblasts, coronary artery smooth muscle cells, small airway epithelium, bronchial epithelium, microvascular dermal endothelial cells, microvascular lung endothelial cells, human pulmonary aortic endothelial cells, human umbilical vein endothelial cells were all purchased from Clonetics (Walkersville, MD) and

grown in the media supplied for these cell types by Clonetics. These primary cell types were activated with various cytokines or combinations of cytokines for 6 and/or 12-14 hours, as indicated. The following cytokines were used; IL-1 beta at approximately 1-5 ng/ml, TNF alpha at approximately 5-10 ng/ml, IFN gamma at approximately 20-50 ng/ml, IL-4 at approximately 5-10 ng/ml, IL-9 at approximately 5-10 ng/ml, IL-13 at approximately 5-10 ng/ml. Endothelial cells were sometimes starved for various times by culture in the basal media from Clonetics with 0.1% serum.

Mononuclear cells were prepared from blood of employees at CuraGen Corporation, using Ficoll. LAK cells were prepared from these cells by culture in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco/Life Technologies, Rockville, MD), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and Interleukin 2 for 4-6 days. Cells were then either activated with 10-20 ng/ml PMA and 1-2 μ g/ml ionomycin, IL-12 at 5-10 ng/ml, IFN gamma at 20-50 ng/ml and IL-18 at 5-10 ng/ml for 6 hours. In some cases, mononuclear cells were cultured for 4-5 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) with PHA (phytohemagglutinin) or PWM (pokeweed mitogen) at approximately 5 μ g/ml. Samples were taken at 24, 48 and 72 hours for RNA preparation. MLR (mixed lymphocyte reaction) samples were obtained by taking blood from two donors, isolating the mononuclear cells using Ficoll and mixing the isolated mononuclear cells 1:1 at a final concentration of approximately 2×10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol (5.5×10^{-5} M) (Gibco), and 10 mM Hepes (Gibco). The MLR was cultured and samples taken at various time points ranging from 1- 7 days for RNA preparation.

Monocytes were isolated from mononuclear cells using CD14 Miltenyi Beads, +ve VS selection columns and a Vario Magnet according to the manufacturer's instructions. Monocytes were differentiated into dendritic cells by culture in DMEM 5% fetal calf serum (FCS) (Hyclone, Logan, UT), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco), 50 ng/ml GMCSF and 5 ng/ml IL-4 for 5-7 days. Macrophages were prepared by culture of monocytes for 5-7 days in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids

(Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco) and 10% AB Human Serum or MCSF at approximately 50 ng/ml. Monocytes, macrophages and dendritic cells were stimulated for 6 and 12-14 hours with lipopolysaccharide (LPS) at 100 ng/ml. Dendritic cells were also stimulated with anti-CD40 monoclonal antibody (Pharmingen) at 10 μ g/ml for 6 and 12-14 hours.

CD4 lymphocytes, CD8 lymphocytes and NK cells were also isolated from mononuclear cells using CD4, CD8 and CD56 Miltenyi beads, positive VS selection columns and a Vario Magnet according to the manufacturer's instructions. CD45RA and CD45RO CD4 lymphocytes were isolated by depleting mononuclear cells of CD8, CD56, CD14 and CD19 cells using CD8, CD56, CD14 and CD19 Miltenyi beads and +ve selection. Then CD45RO beads were used to isolate the CD45RO CD4 lymphocytes with the remaining cells being CD45RA CD4 lymphocytes. CD45RA CD4, CD45RO CD4 and CD8 lymphocytes were placed in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and plated at 10^6 cells/ml onto Falcon 6 well tissue culture plates that had been coated overnight with 0.5 μ g/ml anti-CD28 (Pharmingen) and 3 μ g/ml anti-CD3 (OKT3, ATCC) in PBS. After 6 and 24 hours, the cells were harvested for RNA preparation. To prepare chronically activated CD8 lymphocytes, we activated the isolated CD8 lymphocytes for 4 days on anti-CD28 and anti-CD3 coated plates and then harvested the cells and expanded them in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and IL-2. The expanded CD8 cells were then activated again with plate bound anti-CD3 and anti-CD28 for 4 days and expanded as before. RNA was isolated 6 and 24 hours after the second activation and after 4 days of the second expansion culture. The isolated NK cells were cultured in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco) and IL-2 for 4-6 days before RNA was prepared.

To obtain B cells, tonsils were procured from NDRI. The tonsil was cut up with sterile dissecting scissors and then passed through a sieve. Tonsil cells were then spun down and resuspended at 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10

mM Hepes (Gibco). To activate the cells, we used PWM at 5 µg/ml or anti-CD40 (Pharmingen) at approximately 10 µg/ml and IL-4 at 5-10 ng/ml. Cells were harvested for RNA preparation at 24, 48 and 72 hours.

To prepare the primary and secondary Th1/Th2 and Tr1 cells, six-well Falcon plates were coated overnight with 10 µg/ml anti-CD28 (Pharmingen) and 2 µg/ml OKT3 (ATCC), and then washed twice with PBS. Umbilical cord blood CD4 lymphocytes (Poietic Systems, German Town, MD) were cultured at 10^5 - 10^6 cells/ml in DMEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (4 ng/ml). IL-12 (5 ng/ml) and anti-IL4 (1 µg/ml) were used to direct to Th1, while IL-4 (5 ng/ml) and anti-IFN gamma (1 µg/ml) were used to direct to Th2 and IL-10 at 5 ng/ml was used to direct to Tr1. After 4-5 days, the activated Th1, Th2 and Tr1 lymphocytes were washed once in DMEM and expanded for 4-7 days in DMEM 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco) and IL-2 (1 ng/ml). Following this, the activated Th1, Th2 and Tr1 lymphocytes were re-stimulated for 5 days with anti-CD28/OKT3 and cytokines as described above, but with the addition of anti-CD95L (1 µg/ml) to prevent apoptosis. After 4-5 days, the Th1, Th2 and Tr1 lymphocytes were washed and then expanded again with IL-2 for 4-7 days. Activated Th1 and Th2 lymphocytes were maintained in this way for a maximum of three cycles. RNA was prepared from primary and secondary Th1, Th2 and Tr1 after 6 and 24 hours following the second and third activations with plate bound anti-CD3 and anti-CD28 mAbs and 4 days into the second and third expansion cultures in Interleukin 2.

The following leukocyte cells lines were obtained from the ATCC: Ramos, EOL-1, KU-812. EOL cells were further differentiated by culture in 0.1 mM dbcAMP at 5×10^5 cells/ml for 8 days, changing the media every 3 days and adjusting the cell concentration to 5×10^5 cells/ml. For the culture of these cells, we used DMEM or RPMI (as recommended by the ATCC), with the addition of 5% FCS (Hyclone), 100 µM non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), 10 mM Hepes (Gibco). RNA was either prepared from resting cells or cells activated with PMA at 10 ng/ml and ionomycin at 1 µg/ml for 6 and 14 hours. Keratinocyte line CCD106 and an airway epithelial tumor line NCI-H292 were also obtained from the ATCC. Both were

cultured in DMEM 5% FCS (Hyclone), 100 μ M non essential amino acids (Gibco), 1 mM sodium pyruvate (Gibco), mercaptoethanol 5.5×10^{-5} M (Gibco), and 10 mM Hepes (Gibco). CCD1106 cells were activated for 6 and 14 hours with approximately 5 ng/ml TNF alpha and 1 ng/ml IL-1 beta, while NCI-H292 cells were activated for 6 and 14 hours with the following cytokines: 5 ng/ml IL-4, 5 ng/ml IL-9, 5 ng/ml IL-13 and 25 ng/ml IFN gamma.

For these cell lines and blood cells, RNA was prepared by lysing approximately 10^7 cells/ml using Trizol (Gibco BRL). Briefly, 1/10 volume of bromochloropropane (Molecular Research Corporation) was added to the RNA sample, vortexed and after 10 minutes at room temperature, the tubes were spun at 14,000 rpm in a Sorvall SS34 rotor. The aqueous phase was removed and placed in a 15 ml Falcon Tube. An equal volume of isopropanol was added and left at -20 degrees C overnight. The precipitated RNA was spun down at 9,000 rpm for 15 min in a Sorvall SS34 rotor and washed in 70% ethanol. The pellet was redissolved in 300 μ l of RNase-free water and 35 μ l buffer (Promega) 5 μ l DTT, 7 μ l RNasin and 8 μ l DNase were added. The tube was incubated at 37 degrees C for 30 minutes to remove contaminating genomic DNA, extracted once with phenol chloroform and re-precipitated with 1/10 volume of 3 M sodium acetate and 2 volumes of 100% ethanol. The RNA was spun down and placed in RNase free water. RNA was stored at -80 degrees C.

The above detailed procedures were carried out to obtain the taqman profiles of the clones in question.

Given below are the Primers and the Taqman results for the following clones:

58092213.0.36 – Probe Name: Ag809 (Table 9 and Table 10)

29692275.0.1 – Probe Name: Ag2773 (Table 11 and Table 12)

32125243.0.21 – Probe Name: Ag427 (Table 13 and Table 14)

27455183.0.19 – Probe Name: Ag1541 (Table 15 and Table 16, 17, 18)

Table 8: Primer Design for Probe Ag809 (FCTR1)

Primer	Sequences	TM	Length	Start Pos	SEQID NO
Forward	5'-ATGTGATCTTTGGCTGTGAAGT-3'	58.7	22	337	24
Probe	FAM-5'-CTACCCCATGGCCTCCATCGAGT-3'-TAMRA	69.4	23	365	25

Reverse	5'-GGATGTCCAAGCCATCCTT-3'	59.9	19	393	26
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TABLE 9: TAQMAN RESULTS FOR FCTR1

Tissue_Name	Panel 1	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	79.6	Normal Colon GENPAK 061003	6.8	93768_Secondary Th1_anti-CD28/anti-CD3	2.0
Heart (fetal)	43.8	83219 CC Well to Mod Diff (ODO3866)	6.1	93769_Secondary Th2_anti-CD28/anti-CD3	1.5
Pancreas	2.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	2.5
Pancreatic ca. CAPAN 2	4.7	83221 CC Gr.2 rectosigmoid (ODO3868)	0.9	93573_Secondary Th1_resting day 4-6 in IL-2	1.0
Adrenal gland	2.3	83222 CC NAT (ODO3868)	1.2	93572_Secondary Th2_resting day 4-6 in IL-2	3.0
Thyroid	6.5	83235 CC Mod Diff (ODO3920)	3.8	93571_Secondary Tr1_resting day 4-6 in IL-2	1.7
Salivary gland	12.3	83236 CC NAT (ODO3920)	1.3	93568_primary Th1_anti-CD28/anti-CD3	0.4
Pituitary gland	8.7	83237 CC Gr.2 ascend colon (ODO3921)	6.9	93569_primary Th2_anti-CD28/anti-CD3	1.5
Brain (fetal)	0.0	83238 CC NAT (ODO3921)	4.0	93570_primary Tr1_anti-CD28/anti-CD3	2.0
Brain (whole)	3.0	83241 CC from Partial Hepatectomy (ODO4309)	1.2	93565_primary Th1_resting dy 4-6 in IL-2	5.4
Brain (amygdala)	2.4	83242 Liver NAT (ODO4309)	0.6	93566_primary Th2_resting dy 4-6 in IL-2	3.1
Brain (cerebellum)	0.0	87472 Colon mets to lung (OD04451-01)	4.4	93567_primary Tr1_resting dy 4-6 in IL-2	0.0
Brain (hippocampus)	13.0	87473 Lung NAT (OD04451-02)	1.2	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	11.2
Brain (thalamus)	3.0	Normal Prostate Clontech A+ 6546-1	10.2	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	1.2
Cerebral Cortex	2.3	84140 Prostate Cancer (OD04410)	41.8	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.9
Spinal cord	2.6	84141 Prostate NAT (OD04410)	25.7	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0
CNS ca. (glio/astro) U87-MG	12.1	87073 Prostate Cancer (OD04720-01)	11.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.6
CNS ca. (glio/astro) U-118-MG	100.0	87074 Prostate NAT (OD04720-02)	10.0	93354_CD4_none	1.1
CNS ca. (astro) SW1783	6.5	Normal Lung GENPAK	7.9	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0

		061010			
CNS ca.* (neuro; met) SK-N-AS	52.1	83239 Lung Met to Muscle (ODO4286)	6.5	93103_LAK cells_resting	0.5
CNS ca. (astro) SF-539	12.6	83240 Muscle NAT (ODO4286)	2.6	93788_LAK cells_IL-2	0.0
CNS ca. (astro) SNB-75	11.9	84136 Lung Malignant Cancer (OD03126)	14.8	93787_LAK cells_IL-2+IL-12	0.7
CNS ca. (glio)SNB-19	0.0	84137 Lung NAT (OD03126)	3.2	93789_LAK cells_IL-2+IFN gamma	1.1
CNS ca. (glio)U251	0.9	84871 Lung Cancer (OD04404)	2.1	93790_LAK cells_IL-2+ IL-18	0.3
CNS ca. (glio) SF-295	12.6	84872 Lung NAT (OD04404)	1.9	93104_LAK cells_PMA/ionomycin and IL-18	0.0
Heart	13.9	84875 Lung Cancer (OD04565)	0.3	93578_NK Cells IL-2_resting	1.3
Skeletal muscle	3.2	85950 Lung Cancer (OD04237-01)	1.3	93109_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Bone marrow	3.6	85970 Lung NAT (OD04237-02)	2.6	93110_Mixed Lymphocyte Reaction_Two Way MLR	0.5
Thymus	4.2	83255 Ocular Mel Met to Liver (ODO4310)	0.1	93111_Mixed Lymphocyte Reaction_Two Way MLR	2.7
Spleen	61.6	83256 Liver NAT (ODO4310)	0.6	93112_Mononuclear Cells (PBMCs)_resting	0.0
Lymph node	3.3	84139 Melanoma Mets to Lung (OD04321)	2.5	93113_Mononuclear Cells (PBMCs)_PWM	1.3
Colorectal	11.9	84138 Lung NAT (OD04321)	2.6	93114_Mononuclear Cells (PBMCs)_PHA-L	1.0
Stomach	28.3	Normal Kidney GENPAK 061008	5.6	93249_Ramos (B cell)_none	1.2
Small intestine	4.5	83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.6	93250_Ramos (B cell)_ionomycin	2.3
Colon ca. SW480	46.7	83787 Kidney NAT (OD04338)	3.7	93349_B lymphocytes_PWM	4.3
Colon ca.* (SW480 met)SW620	19.0	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.8	93350_B lymphocytes_CD40L and IL-4	1.4
Colon ca. HT29	5.3	83789 Kidney NAT (OD04339)	3.1	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	7.2
Colon ca. HCT-116	5.0	83790 Kidney Ca, Clear cell type (OD04340)	1.5	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	3.0
Colon ca. CaCo-2	49.3	83791 Kidney NAT (OD04340)	5.1	93356_Dendritic Cells_none	1.5
83219 CC Well to Mod Diff (ODO3866)	3.0	83792 Kidney Ca, Nuclear grade 3	14.5	93355_Dendritic Cells_LPS 100 ng/ml	0.7

		(OD04348)			
Colon ca. HCC-2998	27.7	83793 Kidney NAT (OD04348)	2.5	93775_Dendritic Cells_anti-CD40	0.5
Gastric ca.* (liver met) NCI-N87	10.5	87474 Kidney Cancer (OD04622-01)	1.7	93774_Monocytes_resting	0.5
Bladder	3.7	87475 Kidney NAT (OD04622-03)	2.0	93776_Monocytes_LPS 50 ng/ml	0.0
Trachea	23.5	85973 Kidney Cancer (OD04450-01)	0.3	93581_Macrophages_resting	1.3
Kidney	1.8	85974 Kidney NAT (OD04450-03)	2.0	93582_Macrophages_LPS 100 ng/ml	1.8
Kidney (fetal)	1.9	Kidney Cancer Clontech 8120607	7.0	93098_HUVEC (Endothelial)_none	2.3
Renal ca. 786-0	7.0	Kidney NAT Clontech 8120608	1.5	93099_HUVEC (Endothelial)_starved	9.0
Renal ca. A498	6.8	Kidney Cancer Clontech 8120613	2.0	93100_HUVEC (Endothelial)_IL-1b	1.2
Renal ca.RXF 393	4.7	Kidney NAT Clontech 8120614	4.1	93779_HUVEC (Endothelial)_IFN gamma	1.4
Renal ca.ACHN	9.8	Kidney Cancer Clontech 9010320	2.2	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.8
Renal ca.UO-31	1.3	Kidney NAT Clontech 9010321	3.5	93101_HUVEC (Endothelial)_TNF alpha + IL4	1.1
Renal ca.TK-10	0.6	Normal Uterus GENPAK 061018	3.1	93781_HUVEC (Endothelial)_IL-11	3.0
Liver	0.8	Uterus Cancer GENPAK 064011	17.6	93583_Lung Microvascular Endothelial Cells_none	0.8
Liver (fetal)	1.1	Normal Thyroid Clontech A+ 6570-1	3.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Liver ca. (hepatoblast) HepG2	54.0	Thyroid Cancer GENPAK 064010	1.2	92662_Microvascular Dermal endothelium_none	1.1
Lung	3.9	Thyroid Cancer INVITROGEN A302152	0.6	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.0
Lung (fetal)	9.0	Thyroid NAT INVITROGEN A302153	2.6	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0
Lung ca. (small cell) LX-1	34.4	Normal Breast GENPAK 061019	3.4	93347_Small Airway Epithelium_none	0.4
Lung ca. (small cell) NCI-H69	3.0	84877 Breast Cancer (OD04566)	0.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.5
Lung ca. (s.cell var.) SHP-77	13.0	85975 Breast Cancer	67.8	92668_Coronary Artery SMC_resting	5.8

		(OD04590-01)			
Lung ca. (large cell) NCI-H460	6.8	85976 Breast Cancer Mets (OD04590-03)	51.1	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.3
Lung ca. (non-sm. cell) A549	3.4	87070 Breast Cancer Metastasis (OD04655-05)	12.7	93107_astrocytes_resting	2.7
Lung ca. (non-s.cell) NCI-H23	34.4	GENPAK Breast Cancer 064006	8.9	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0
Lung ca (non-s.cell) HOP-62	10.5	Breast Cancer Clontech 9100266	6.2	92666_KU-812 (Basophil)_resting	6.8
Lung ca. (non-s.cl) NCI-H522	47.6	Breast NAT Clontech 9100265	3.3	92667_KU-812 (Basophil)_PMA/ionoycin	8.4
Lung ca. (squam.) SW 900	4.7	Breast Cancer INVITROGEN A209073	3.4	93579_CCD1106 (Keratinocytes)_none	1.6
Lung ca. (squam.) NCI-H596	0.7	Breast NAT INVITROGEN A2090734	8.7	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	1.4
Mammary gland	9.9	Normal Liver GENPAK 061009	1.1	93791_Liver Cirrhosis	4.2
Breast ca.* (pl. effusion) MCF-7	5.6	Liver Cancer GENPAK 064003	0.6	93792_Lupus Kidney	1.9
Breast ca.* (pl.ef) MDA-MB-231	21.3	Liver Cancer Research Genetics RNA 1025	0.6	93577_NCI-H292	39.5
Breast ca.* (pl. effusion) T47D	66.0	Liver Cancer Research Genetics RNA 1026	1.4	93358_NCI-H292_IL-4	39.0
Breast ca. BT-549	7.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	1.3	93360_NCI-H292_IL-9	65.5
Breast ca.MDA-N	18.7	Paired Liver Tissue Research Genetics RNA 6004-N	1.3	93359_NCI-H292_IL-13	37.1
Ovary	12.1	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	1.1	93357_NCI-H292_IFN gamma	31.9
Ovarian ca.OVCAR-3	3.5	Paired Liver Tissue Research Genetics RNA 6005-N	0.3	93777_HPAEC -	0.5
Ovarian ca.OVCAR-4	4.0	Normal Bladder GENPAK 061001	5.9	93778_HPAEC_IL-1 beta/TNA alpha	1.2
Ovarian ca. OVCAR-5	9.1	Bladder Cancer Research	1.7	93254_Normal Human Lung Fibroblast_none	42.3

		Genetics RNA 1023			
Ovarian ca. OVCAR-8	12.7	Bladder Cancer INVITROGEN A302173	1.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	17.8
Ovarian ca.IGROV-1	9.8	87071 Bladder Cancer (OD04718-01)	2.0	93257_Normal Human Lung Fibroblast_IL-4	100.0
Ovarian ca.* (ascites) SK-OV-3	0.4	87072 Bladder Normal Adjacent (OD04718-03)	3.3	93256_Normal Human Lung Fibroblast_IL-9	72.7
Uterus	6.9	Normal Ovary Res. Gen.	2.2	93255_Normal Human Lung Fibroblast_IL-13	60.7
Placenta	4.6	Ovarian Cancer GENPAK 064008	29.1	93258_Normal Human Lung Fibroblast_IFN gamma	81.8
Prostate	15.7	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	76.8
Prostate ca.* (bone met)PC-3	35.9	87493 Ovary NAT (OD04768-08)	2.2	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	30.2
Testis	14.6	Normal Stomach GENPAK 061017	13.1	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	38.2
Melanoma Hs688(A).T	13.5	NAT Stomach Clontech 9060359	8.8	93772_dermal fibroblast_IFN gamma	34.2
Melanoma* (met) Hs688(B).T	71.2	Gastric Cancer Clontech 9060395	2.5	93771_dermal fibroblast_IL-4	80.7
Melanoma UACC-62	1.7	NAT Stomach Clontech 9060394	9.7	93259_IBD Colitis 1**	0.0
Melanoma M14	9.5	Gastric Cancer Clontech 9060397	15.9	93260_IBD Colitis 2	0.3
Melanoma LOX IMVI	2.4	NAT Stomach Clontech 9060396	12.9	93261_IBD Crohns	1.4
Melanoma* (met)SK-MEL-5	3.4	Gastric Cancer GENPAK 064005	12.1	735010_Colon_normal	35.6
Adipose	5.9			735019_Lung_none	11.0
				64028-1_Thymus_none	5.8
				64030-1_Kidney_none	9.7

Taqman results shown in Table 9 demonstrates that cFCTR1 is highly expressed by tumor cell lines and also overexpressed in tumor tissues, specifically breast and ovarian tumor compared to Normal Adjacent Tissues (NAT). There are reports that follistatin can act as a modulator of tumor growth and its expression also correlate with polycystic ovary syndrome, a benign form of ovarian tumor.

Table 10: Primer Design for Probe Ag2773 (FCTR4)

Primer	Sequences	TM	Length	Start Pos	SEQ ID NO
Forward	5'-CCTTGCTTTGTCATATGCTGTT-3'	59.3	22	243	29
Probe	FAM-5'-CCCTTTCCTGGAATATAAACTCTCA-3'-TAMRA	64.6	26	265	30
Reverse	5'-AGAGGAAGCTTTCTGGAGAAGA-3'	58.9	22	313	31

TABLE 11: TAQMAN RESULTS FOR CLONE FCTR4

Tissue_Name	Panel 1D	Tissue_Name	Panel 2D	Tissue_Name	Panel 4D
Liver adenocarcinoma	18.3	Normal Colon GENPAK 061003	41.2	93768_Secondary Th1_anti-CD28/anti-CD3	12.7
Heart (fetal)	4.3	83219 CC Well to Mod Diff (ODO3866)	5.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.2
Pancreas	3.1	83220 CC NAT (ODO3866)	2.5	93770_Secondary Tr1_anti-CD28/anti-CD3	14.7
Pancreatic ca.CAPAN 2	20.0	83221 CC Gr.2 rectosigmoid (ODO3868)	0.7	93573_Secondary Th1_resting day 4-6 in IL-2	4.7
Adrenal gland	7.4	83222 CC NAT (ODO3868)	1.4	93572_Secondary Th2_resting day 4-6 in IL-2	3.5
Thyroid	6.8	83235 CC Mod Diff (ODO3920)	14.0	93571_Secondary Tr1_resting day 4-6 in IL-2	7.0
Salivary gland	2.5	83236 CC NAT (ODO3920)	13.9	93568_primary Th1_anti-CD28/anti-CD3	22.4
Pituitary gland	5.7	83237 CC Gr.2 ascend colon (ODO3921)	16.2	93569_primary Th2_anti-CD28/anti-CD3	16.3
Brain (fetal)	14.4	83238 CC NAT (ODO3921)	5.2	93570_primary Tr1_anti-CD28/anti-CD3	21.8
Brain (whole)	19.6	83241 CC from Partial Hepatectomy (ODO4309)	13.9	93565_primary Th1_resting dy 4-6 in IL-2	30.2
Brain (amygdala)	3.7	83242 Liver NAT (ODO4309)	12.7	93566_primary Th2_resting dy 4-6 in IL-2	14.4
Brain (cerebellum)	2.1	87472 Colon mets to lung (OD04451-01)	3.4	93567_primary Tr1_resting dy 4-6 in IL-2	7.4
Brain (hippocampus)	22.7	87473 Lung NAT (OD04451-02)	1.5	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	7.6
Brain (thalamus)	7.4	Normal Prostate Clontech A+ 6546-1	1.0	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	11.1
Cerebral Cortex	47.3	84140 Prostate Cancer (OD04410)	3.1	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.6
Spinal cord	8.3	84141 Prostate NAT (OD04410)	10.6	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	9.7
CNS ca. (glio/astro)U87-MG	19.9	87073 Prostate Cancer (OD04720-01)	9.7	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	6.2
CNS ca. (glio/astro) U-	57.0	87074 Prostate NAT (OD04720-	8.3	93354_CD4_none	6.4

118-MG		02)			
CNS ca. (astro) SW1783	10.0	Normal Lung GENPAK 061010	36.6	93252_Secondary Th1/Th2/Tr1_anti- CD95 CH11	9.3
CNS ca.* (neuro; met)SK- N-AS	44.8	83239 Lung Met to Muscle (ODO4286)	11.7	93103_LAK cells_resting	11.0
CNS ca. (astro) SF-539	37.4	83240 Muscle NAT (ODO4286)	3.4	93788_LAK cells_IL-2	10.4
CNS ca. (astro) SNB-75	62.0	84136 Lung Malignant Cancer (OD03126)	15.1	93787_LAK cells_IL-2+IL-12	7.4
CNS ca. (glio) SNB-19	24.8	84137 Lung NAT (OD03126)	17.4	93789_LAK cells_IL-2+IFN gamma	11.6
CNS ca. (glio) U251	40.3	84871 Lung Cancer (OD04404)	5.0	93790_LAK cells_IL-2+ IL-18	13.3
CNS ca. (glio) SF-295	100.0	84872 Lung NAT (OD04404)	6.3	93104_LAK cells_PMA/ionomycin and IL-18	4.8
Heart	0.0	84875 Lung Cancer (OD04565)	3.2	93578_NK Cells IL-2_resting	6.2
Skeletal muscle	0.0	85950 Lung Cancer (OD04237-01)	15.8	93109_Mixed Lymphocyte Reaction_Two Way MLR	12.3
Bone marrow	33.7	85970 Lung NAT (OD04237-02)	10.5	93110_Mixed Lymphocyte Reaction_Two Way MLR	8.7
Thymus	12.4	83255 Ocular Mel Met to Liver (ODO4310)	5.9	93111_Mixed Lymphocyte Reaction_Two Way MLR	3.5
Spleen	21.3	83256 Liver NAT (ODO4310)	3.6	93112_Mononuclear Cells (PBMCs)_resting	4.5
Lymph node	13.4	84139 Melanoma Mets to Lung (OD04321)	10.6	93113_Mononuclear Cells (PBMCs)_PWM	21.2
Colorectal	38.2	84138 Lung NAT (OD04321)	10.6	93114_Mononuclear Cells (PBMCs)_PHA-L	8.9
Stomach	9.9	Normal Kidney GENPAK 061008	26.2	93249_Ramos (B cell)_none	100.0
Small intestine	17.9	83786 Kidney Ca, Nuclear grade 2 (OD04338)	22.2	93250_Ramos (B cell)_ionomycin	28.7
Colon ca.SW480	27.7	83787 Kidney NAT (OD04338)	11.7	93349_B lymphocytes_PWM	20.0
Colon ca.* (SW480 met)SW620	30.8	83788 Kidney Ca Nuclear grade 1/2 (OD04339)	45.1	93350_B lymphocytes_CD40L and IL- 4	7.8
Colon ca.HT29	8.1	83789 Kidney NAT (OD04339)	14.8	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	8.0
Colon ca.HCT- 116	35.4	83790 Kidney Ca, Clear cell type (OD04340)	26.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	3.8
Colon ca. CaCo- 2	37.6	83791 Kidney NAT (OD04340)	10.4	93356_Dendritic Cells_none	6.8
83219 CC Well to Mod Diff (ODO3866)	17.8	83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.4	93355_Dendritic Cells_LPS 100 ng/ml	3.3
Colon ca.HCC-	19.9	83793 Kidney	18.8	93775_Dendritic Cells_anti-CD40	6.3

2998		NAT (OD04348)			
Gastric ca.* (liver met) NCI-N87	73.2	87474 Kidney Cancer (OD04622-01)	5.6	93774_Monocytes_resting	10.6
Bladder	43.2	87475 Kidney NAT (OD04622-03)	0.5	93776_Monocytes_LPS 50 ng/ml	3.5
Trachea	10.3	85973 Kidney Cancer (OD04450-01)	21.2	93581_Macrophages_resting	7.6
Kidney	9.2	85974 Kidney NAT (OD04450-03)	9.3	93582_Macrophages_LPS 100 ng/ml	3.9
Kidney (fetal)	0.0	Kidney Cancer Clontech 8120607	0.0	93098_HUVEC (Endothelial)_none	8.5
Renal ca.786-0	53.6	Kidney NAT Clontech 8120608	0.9	93099_HUVEC (Endothelial)_starved	17.9
Renal ca. A498	36.1	Kidney Cancer Clontech 8120613	0.0	93100_HUVEC (Endothelial)_IL-1b	6.0
Renal ca.RXF 393	31.6	Kidney NAT Clontech 8120614	0.9	93779_HUVEC (Endothelial)_IFN gamma	7.8
Renal ca.ACHN	21.6	Kidney Cancer Clontech 9010320	2.7	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	5.7
Renal ca.UO-31	28.7	Kidney NAT Clontech 9010321	5.0	93101_HUVEC (Endothelial)_TNF alpha + IL4	5.6
Renal ca.TK-10	7.0	Normal Uterus GENPAK 061018	5.3	93781_HUVEC (Endothelial)_IL-11	4.9
Liver	14.2	Uterus Cancer GENPAK 064011	9.0	93583_Lung Microvascular Endothelial Cells_none	4.9
Liver (fetal)	14.5	Normal Thyroid Clontech A+ 6570-1	3.4	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	4.9
Liver ca. (hepatoblast) HepG2	59.9	Thyroid Cancer GENPAK 064010	1.8	92662_Microvascular Dermal endothelium_none	8.6
Lung	17.8	Thyroid Cancer INVITROGEN A302152	3.6	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	6.0
Lung (fetal)	9.6	Thyroid NAT INVITROGEN A302153	4.9	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.9
Lung ca. (small cell) LX-1	70.2	Normal Breast GENPAK 061019	8.5	93347_Small Airway Epithelium_none	1.3
Lung ca. (small cell) NCI-H69	29.9	84877 Breast Cancer (OD04566)	1.5	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	13.2
Lung ca. (s.cell var.) SHP-77	3.9	85975 Breast Cancer (OD04590-01)	23.8	92668_Coronary Artery SMC_resting	3.4
Lung ca. (large cell)NCI-H460	2.0	85976 Breast Cancer Mets (OD04590-03)	24.5	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	2.0
Lung ca. (non-	28.5	87070 Breast	12.9	93107_astrocytes resting	4.7

sm. cell) A549		Cancer Metastasis (OD04655-05)			
Lung ca. (non-s.cell) NCI-H23	36.1	GENPAK Breast Cancer 064006	11.8	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	1.9
Lung ca (non-s.cell) HOP-62	29.9	Breast Cancer Clontech 9100266	3.2	92666_KU-812 (Basophil)_resting	5.8
Lung ca. (non-s.c) NCI-H522	17.2	Breast NAT Clontech 9100265	1.8	92667_KU-812 (Basophil)_PMA/ionoycin	12.0
Lung ca. (squam.) SW 900	63.7	Breast Cancer INVITROGEN A209073	11.0	93579_CCD1106 (Keratinocytes)_none	4.9
Lung ca. (squam.) NCI-H596	10.0	Breast NAT INVITROGEN A2090734	7.1	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	0.3
Mammary gland	4.6	Normal Liver GENPAK 061009	8.8	93791_Liver Cirrhosis	1.8
Breast ca.* (pl. effusion) MCF-7	0.0	Liver Cancer GENPAK 064003	4.9	93792_Lupus Kidney	1.6
Breast ca.* (pl.ef) MDA-MB-231	38.7	Liver Cancer Research Genetics RNA 1025	1.0	93577_NCI-H292	11.1
Breast ca.* (pl. effusion) T47D	0.0	Liver Cancer Research Genetics RNA 1026	0.8	93358_NCI-H292_IL-4	12.2
Breast ca.BT-549	4.6	Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.0	93360_NCI-H292_IL-9	7.6
Breast ca.MDA-N	19.0	Paired Liver Tissue Research Genetics RNA 6004-N	7.3	93359_NCI-H292_IL-13	6.1
Ovary	1.7	Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.2	93357_NCI-H292_IFN gamma	5.8
Ovarian ca.OVCAR-3	4.8	Paired Liver Tissue Research Genetics RNA 6005-N	0.0	93777_HPAEC_-	6.8
Ovarian ca.OVCAR-4	0.0	Normal Bladder GENPAK 061001	19.8	93778_HPAEC_IL-1 beta/TNA alpha	5.4
Ovarian ca.OVCAR-5	39.0	Bladder Cancer Research Genetics RNA 1023	3.1	93254_Normal Human Lung Fibroblast_none	2.1
Ovarian ca.OVCAR-8	36.6	Bladder Cancer INVITROGEN A302173	9.9	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	1.9
Ovarian ca.IGROV-1	0.0	87071 Bladder Cancer	6.6	93257_Normal Human Lung Fibroblast_IL-4	3.6

		(OD04718-01)			
Ovarian ca.* (ascites) SK- OV-3	65.5	87072 Bladder Normal Adjacent (OD04718-03)	4.0	93256_Normal Human Lung Fibroblast_IL-9	3.3
Uterus	1.6	Normal Ovary Res. Gen.	0.3	93255_Normal Human Lung Fibroblast_IL-13	2.3
Placenta	8.9	Ovarian Cancer GENPAK 064008	6.8	93258_Normal Human Lung Fibroblast_IFN gamma	2.9
Prostate	0.0	87492 Ovary Cancer (OD04768-07)	100.0	93106_Dermal Fibroblasts CCD1070_resting	5.6
Prostate ca.* (bone met)PC-3	9.2	87493 Ovary NAT (OD04768- 08)	3.6	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	17.4
Testis	29.5	Normal Stomach GENPAK 061017	8.6	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	3.8
Melanoma Hs688(A).T	14.3	NAT Stomach Clontech 9060359	0.7	93772_dermal fibroblast_IFN gamma	2.6
Melanoma* (met) Hs688(B).T	22.9	Gastric Cancer Clontech 9060395	3.9	93771_dermal fibroblast_IL-4	3.4
Melanoma UACC-62	9.7	NAT Stomach Clontech 9060394	5.3	93259_IBD Colitis 1**	0.2
Melanoma M14	12.7	Gastric Cancer Clontech 9060397	13.2	93260_IBD Colitis 2	0.4
Melanoma LOX IMVI	4.5	NAT Stomach Clontech 9060396	1.1	93261_IBD Crohns	0.3
Melanoma* (met) SK-MEL-5	21.8	Gastric Cancer GENPAK 064005	23.0	735010_Colon_normal	3.3
Adipose	6.7			735019_Lung_none	3.9
				64028-1_Thymus_none	7.7
				64030-1_Kidney_none	21.8

Table 12 shows the taqman results of clone FCTR4 indicating overexpression in ovarian cancer as compared to Normal Adjacent Tissue (NAT). In addition, increased expression is demonstrated by ovarian tumor cell line suggesting that antibodies could be used to treat ovarian tumors.

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Table 13: Primer Design for Probe Ag427 (FCTR5)

Primer	Sequences	Length	Start Pos	SEQ ID NO
Forward	5'-GAGCTACAGGCAGCCTCGAGT-3'	21	443	32
Probe	TET-5'-TGGCCCAGCTGACCCTGCTCA-3'-TAMRA	21		33
Reverse	5'-GGCTACGTCAGTGGGTTTGG-3'	20	449	34

Table 14: Taqman results for FCTR5

Tissue_Name	Panel 1	Tissue_Name	Panel 4D
Endothelial cells	10.7	93768_Secondary Th1_anti-CD28/anti-CD3	15.9
Endothelial cells (treated)	15.2	93769_Secondary Th2_anti-CD28/anti-CD3	14.7
Pancreas	16.2	93770_Secondary Tr1_anti-CD28/anti-CD3	21.9
Pancreatic ca.CAPAN 2	10.5	93573_Secondary Th1_resting day 4-6 in IL-2	12.3
Adipose	45.1	93572_Secondary Th2_resting day 4-6 in IL-2	16.2
Adrenal gland	61.6	93571_Secondary Tr1_resting day 4-6 in IL-2	16.2
Thyroid	13.1	93568_primary Th1_anti-CD28/anti-CD3	13.9
Salavary gland	33.7	93569_primary Th2_anti-CD28/anti-CD3	14.6
Pituitary gland	15.8	93570_primary Tr1_anti-CD28/anti-CD3	26.2
Brain (fetal)	7.2	93565_primary Th1_resting dy 4-6 in IL-2	56.3
Brain (whole)	6.3	93566_primary Th2_resting dy 4-6 in IL-2	27.7
Brain (amygdala)	8.4	93567_primary Tr1_resting dy 4-6 in IL-2	31.6
Brain (cerebellum)	6.8	93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	12.1
Brain (hippocampus)	7.9	93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	17.1
Brain (substantia nigra)	9.5	93251_CD8 Lymphocytes_anti-CD28/anti-CD3	9.1
Brain (thalamus)	7.9	93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	13.4
Brain (hypothalamus)	23.0	93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	9.2
Spinal cord	9.5	93354_CD4_none	7.6
CNS ca. (glio/astro)U87-MG	12.6	93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	20.2
CNS ca. (glio/astro)U-118-MG	11.6	93103_LAK cells_resting	57.0
CNS ca. (astro)SW1783	4.3	93788_LAK cells_IL-2	18.8
CNS ca.* (neuro; met)SK-N-AS	10.4	93787_LAK cells_IL-2+IL-12	14.2
CNS ca. (astro) SF-539	11.6	93789_LAK cells_IL-2+IFN gamma	20.9
CNS ca. (astro) SNB-75	4.4	93790_LAK cells_IL-2+ IL-18	14.8
CNS ca. (glio)SNB-19	31.6	93104_LAK cells_PMA/ionomycin and IL-18	12.9
CNS ca. (glio)U251	17.3	93578_NK Cells IL-2_resting	17.4
CNS ca. (glio)SF-295	20.9	93109_Mixed Lymphocyte Reaction_Two Way MLR	43.5
Heart	14.3	93110_Mixed Lymphocyte Reaction_Two Way MLR	19.3
Skeletal muscle	11.7	93111_Mixed Lymphocyte Reaction_Two Way MLR	12.6
Bone marrow	21.9	93112_Mononuclear Cells (PBMCs)_resting	8.7
Thymus	20.9	93113_Mononuclear Cells (PBMCs)_PWM	28.5
Spleen	23.8	93114_Mononuclear Cells (PBMCs)_PHA-L	26.2
Lymph node	24.2	93249_Ramos (B cell)_none	0.3
Colon (ascending)	17.2	93250_Ramos (B cell)_ionomycin	1.2
Stomach	11.1	93349_B lymphocytes_PWM	25.7
Small intestine	21.5	93350_B lymphocytes_CD40L and IL-4	13.0

Colon ca.SW480	12.2	92665_EOL-1 (Eosinophil)_dbcAMP differentiated	26.4
Colon ca.* (SW480 met)SW620	8.6	93248_EOL-1 (Eosinophil)_dbcAMP/PMAionomycin	11.4
Colon ca.HT29	16.2	93356_Dendritic Cells_none	40.3
Colon ca.HCT-116	8.1	93355_Dendritic Cells_LPS 100 ng/ml	33.0
Colon ca.CaCo-2	22.1	93775_Dendritic Cells_anti-CD40	20.5
Colon ca.HCT-15	18.6	93774_Monocytes_resting	23.3
Colon ca.HCC-2998	21.9	93776_Monocytes_LPS 50 ng/ml	6.9
Gastric ca.* (liver met) NCI-N87	42.9	93581_Macrophages_resting	14.7
Bladder	95.3	93582_Macrophages_LPS 100 ng/ml	64.6
Trachea	18.3	93098_HUVEC (Endothelial)_none	6.8
Kidney	25.7	93099_HUVEC (Endothelial)_starved	13.9
Kidney (fetal)	15.8	93100_HUVEC (Endothelial)_IL-1b	7.5
Renal ca.786-0	16.5	93779_HUVEC (Endothelial)_IFN gamma	27.7
Renal ca.A498	16.5	93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	11.8
Renal ca.RXF 393	7.4	93101_HUVEC (Endothelial)_TNF alpha + IL4	6.7
Renal ca.ACHN	11.9	93781_HUVEC (Endothelial)_IL-11	10.4
Renal ca.UO-31	15.8	93583_Lung Microvascular Endothelial Cells_none	8.8
Renal ca.TK-10	28.7	93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	8.6
Liver	100.0	92662_Microvascular Dermal endothelium_none	22.1
Liver (fetal)	81.8	92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	18.7
Liver ca. (hepatoblast) HepG2	28.3	93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	35.4
Lung	10.7	93347_Small Airway Epithelium_none	10.9
Lung (fetal)	10.9	93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	50.0
Lung ca. (small cell) LX-1	24.3	92668_Coronary Artery SMC_resting	27.9
Lung ca. (small cell) NCI-H69	41.5	92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	25.4
Lung ca. (s.cell var.) SHP-77	4.6	93107_astrocytes_resting	7.4
Lung ca. (large cell)NCI-H460	46.3	93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	10.7
Lung ca. (non-sm. cell) A549	45.4	92666_KU-812 (Basophil)_resting	3.2
Lung ca. (non-s.cell) NCI-H23	54.3	92667_KU-812 (Basophil)_PMA/ionomycin	6.7
Lung ca (non-s.cell) HOP-62	50.7	93579_CCD1106 (Keratinocytes)_none	12.2
Lung ca. (non-s.cl) NCI-H522	38.4	93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	100.0
Lung ca. (squam.) SW 900	30.8	93791_Liver Cirrhosis	27.6
Lung ca. (squam.) NCI-H596	15.5	93792_Lupus Kidney	32.3
Mammary gland	65.5	93577_NCI-H292	77.4
Breast ca.* (pl. effusion) MCF-7	4.4	93358_NCI-H292_IL-4	70.2
Breast ca.* (pl.ef) MDA-MB-231	3.5	93360_NCI-H292_IL-9	54.3
Breast ca.* (pl. effusion)T47D	8.7	93359_NCI-H292_IL-13	47.0
Breast ca. BT-549	5.7	93357_NCI-H292_IFN gamma	52.9
Breast ca.MDA-N	16.6	93777_HPAEC_-	23.8
Ovary	20.5	93778_HPAEC_IL-1 beta/TNA alpha	21.5

Ovarian ca. OVCAR-3	21.6	93254_Normal Human Lung Fibroblast_none	49.3
Ovarian ca.OVCAR-4	8.3	93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	40.3
Ovarian ca.OVCAR-5	26.1	93257_Normal Human Lung Fibroblast_IL-4	48.3
Ovarian ca.OVCAR-8	48.0	93256_Normal Human Lung Fibroblast_IL-9	29.3
Ovarian ca.IGROV-1	9.3	93255_Normal Human Lung Fibroblast_IL-13	73.7
Ovarian ca.* (ascites)SK-OV-3	8.8	93258_Normal Human Lung Fibroblast_IFN gamma	66.9
Uterus	13.4	93106_Dermal Fibroblasts CCD1070_resting	20.2
Placenta	9.4	93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	35.1
Prostate	21.3	93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	15.0
Prostate ca.* (bone met)PC-3	17.7	93772_dermal fibroblast_IFN gamma	21.8
Testis	11.7	93771_dermal fibroblast_IL-4	21.2
Melanoma Hs688(A).T	9.0	93259_IBD Colitis 1**	8.8
Melanoma* (met) Hs688(B).T	12.9	93260_IBD Colitis 2	3.5
Melanoma UACC-62	12.4	93261_IBD Crohns	1.3
Melanoma M14	9.5	735010_Colon_normal	20.3
Melanoma LOX IMVI	8.1	735019_Lung_none	40.3
Melanoma* (met) SK-MEL-5	8.8	64028-1_Thymus_none	33.5
Melanoma SK-MEL-28	8.0	64030-1_Kidney_none	21.0

Taqman results in Table 14 show high expression of clone FCTR5 in bladder, liver and adrenal gland suggesting a possible role in the treatment of diseases involving these tissues.

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Table 15: Primer Design for Probe Ag1541 (FCTR6)

Primer	Sequences	TM	Length	Start Pos.	SEQ ID NO
Forward	5'-AGAAGAACACCCAGGGATATA-3'	58.8	22	1076	35
Probe	FAM-5'-CCTCGTTGGTGAACCTACAACCTCTGG-3'-TAMRA	67.9	26	1100	36
Reverse	5'-CCTCTAGCTGGGTCACTTTCTC-3'	59.5	22	1129	37

TABLE 16: TAQMAN RESULTS FOR FCTR6 (PANEL 1D)

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Tissue_Name	Panel 1D	
	Run 1	Run 2
Liver adenocarcinoma	0.0	0.0
Heart (fetal)	0.0	0.0
Pancreas	0.0	0.0

Pancreatic ca.CAPAN 2	0.0	0.0
Adrenal gland	0.0	0.0
Thyroid	0.0	0.0
Salivary gland	0.0	0.0
Pituitary gland	0.0	0.0
Brain (fetal)	0.5	0.4
Brain (whole)	1.1	1.7
Brain (amygdala)	0.0	1.8
Brain (cerebellum)	0.6	1.9
Brain (hippocampus)	3.3	3.4
Brain (thalamus)	1.0	1.2
Cerebral Cortex	1.6	2.6
Spinal cord	2.5	0.4
CNS ca. (glio/astro)U87-MG	0.0	0.0
CNS ca. (glio/astro)U-118-MG	0.0	0.0
CNS ca. (astro)SW1783	0.0	0.0
CNS ca.* (neuro; met)SK-N-AS	0.0	0.0
CNS ca. (astro)SF-539	0.0	0.0
CNS ca. (astro) SNB-75	0.7	0.0
CNS ca. (glio)SNB-19	0.0	0.0
CNS ca. (glio)U251	0.0	0.0
CNS ca. (glio)SF-295	0.0	0.8
Heart	0.0	0.0
Skeletal muscle	0.0	0.0
Bone marrow	0.0	0.0
Thymus	0.0	0.0
Spleen	0.0	0.0
Lymph node	0.0	0.0
Colorectal	0.0	0.6
Stomach	1.9	0.0
Small intestine	0.0	1.0
Colon ca. SW480	0.0	0.0
Colon ca.* (SW480 met)SW620	0.0	0.0
Colon ca. HT29	0.0	0.0
Colon ca. HCT-116	0.6	0.4
Colon ca.CaCo-2	1.5	0.0
83219 CC Well to Mod Diff (ODO3866)	0.0	0.0
Colon ca.HCC-2998	0.0	0.0
Gastric ca.* (liver met) NCI-N87	1.2	0.0
Bladder	0.0	0.0
Trachea	0.0	0.4
Kidney	0.8	1.2
Kidney (fetal)	0.5	0.7
Renal ca.786-0	0.0	0.0
Renal ca.A498	0.0	0.0
Renal ca.RXF 393	0.0	0.0
Renal ca.ACHN	0.0	0.0
Renal ca. UO-31	0.0	0.0
Renal ca.TK-10	0.0	0.0
Liver	0.0	0.0
Liver (fetal)	0.2	0.0
Liver ca. (hepatoblast) HepG2	0.0	0.0
Lung	0.0	0.0
Lung (fetal)	0.0	0.0
Lung ca. (small cell) LX-1	1.7	2.3
Lung ca. (small cell)NCI-H69	0.0	0.0
Lung ca. (s.cell var.) SHP-77	1.3	2.5
Lung ca. (large cell)NCI-H460	0.0	0.0

Lung ca. (non-sm. cell) A549	0.0	0.0
Lung ca. (non-s.cell) NCI-H23	1.2	0.4
Lung ca (non-s.cell) HOP-62	0.0	0.0
Lung ca. (non-s.cl) NCI-H522	0.0	0.0
Lung ca. (squam.) SW 900	0.0	0.7
Lung ca. (squam.) NCI-H596	0.0	1.3
Mammary gland	0.0	1.5
Breast ca.* (pl. effusion) MCF-7	0.0	0.0
Breast ca.* (pl.ef) MDA-MB-231	5.8	0.5
Breast ca.* (pl. effusion) T47D	1.2	0.3
Breast ca. BT-549	0.5	0.0
Breast ca. MDA-N	0.0	0.0
Ovary	0.0	0.0
Ovarian ca. OVCAR-3	0.0	0.0
Ovarian ca.OVCAR-4	0.0	0.0
Ovarian ca.OVCAR-5	3.6	0.7
Ovarian ca.OVCAR-8	0.0	0.0
Ovarian ca.IGROV-1	0.0	0.0
Ovarian ca.* (ascites) SK-OV-3	0.0	0.0
Uterus	0.0	0.0
Placenta	0.0	0.0
Prostate	0.0	0.7
Prostate ca.* (bone met)PC-3	0.0	0.0
Testis	100.0	100.0
Melanoma Hs688(A).T	0.0	0.0
Melanoma* (met) Hs688(B).T	0.0	0.0
Melanoma UACC-62	0.0	0.0
Melanoma M14	0.0	0.0
Melanoma LOX IMVI	0.0	0.0
Melanoma* (met)SK-MEL-5	0.0	0.0
Adipose	0.5	0.0

Table 17: Taqman Results for FCTR6 (Panel 2D)

Tissue_Name	Panel 2D	
	Run 1	Run 2
Normal Colon GENPAK 061003	5.4	2.4
83219 CC Well to Mod Diff (ODO3866)	7.3	0.0
83220 CC NAT (ODO3866)	5.8	1.5
83221 CC Gr.2 rectosigmoid (ODO3868)	3.4	0.0
83222 CC NAT (ODO3868)	0.0	0.0
83235 CC Mod Diff (ODO3920)	11.0	1.4
83236 CC NAT (ODO3920)	0.0	0.0
83237 CC Gr.2 ascend colon (ODO3921)	6.2	2.5
83238 CC NAT (ODO3921)	10.2	0.0
83241 CC from Partial Hepatectomy (ODO4309)	3.6	0.0
83242 Liver NAT (ODO4309)	0.0	2.4
87472 Colon mets to lung (OD04451-01)	7.2	4.4
87473 Lung NAT (OD04451-02)	0.0	0.0
Normal Prostate Clontech A+ 6546-1	4.8	2.9
84140 Prostate Cancer (OD04410)	3.5	0.0
84141 Prostate NAT (OD04410)	3.4	0.0
87073 Prostate Cancer (OD04720-01)	9.0	8.5
87074 Prostate NAT (OD04720-02)	0.0	0.0
Normal Lung GENPAK 061010	17.7	6.5

83239 Lung Met to Muscle (ODO4286)	0.0	2.3
83240 Muscle NAT (ODO4286)	0.0	0.0
84136 Lung Malignant Cancer (OD03126)	6.5	5.7
84137 Lung NAT (OD03126)	0.0	0.0
84871 Lung Cancer (OD04404)	0.0	0.0
84872 Lung NAT (OD04404)	0.0	0.0
84875 Lung Cancer (OD04565)	0.0	0.0
85950 Lung Cancer (OD04237-01)	0.0	0.0
85970 Lung NAT (OD04237-02)	0.0	0.0
83255 Ocular Mel Met to Liver (ODO4310)	4.3	0.0
83256 Liver NAT (ODO4310)	0.0	0.0
84139 Melanoma Mets to Lung (OD04321)	0.0	0.0
84138 Lung NAT (OD04321)	0.0	0.0
Normal Kidney GENPAK 061008	28.1	39.2
83786 Kidney Ca, Nuclear grade 2 (OD04338)	0.0	3.0
83787 Kidney NAT (OD04338)	22.7	31.6
83788 Kidney Ca Nuclear grade 1/2 (OD04339)	0.0	3.1
83789 Kidney NAT (OD04339)	97.3	100.0
83790 Kidney Ca, Clear cell type (OD04340)	0.0	0.0
83791 Kidney NAT (OD04340)	100.0	34.4
83792 Kidney Ca, Nuclear grade 3 (OD04348)	2.0	4.9
83793 Kidney NAT (OD04348)	30.2	19.9
87474 Kidney Cancer (OD04622-01)	0.0	2.4
87475 Kidney NAT (OD04622-03)	8.4	7.2
85973 Kidney Cancer (OD04450-01)	0.0	0.0
85974 Kidney NAT (OD04450-03)	47.3	12.9
Kidney Cancer Clontech 8120607	0.0	0.0
Kidney NAT Clontech 8120608	0.0	0.0
Kidney Cancer Clontech 8120613	0.0	0.0
Kidney NAT Clontech 8120614	20.6	22.9
Kidney Cancer Clontech 9010320	0.0	0.0
Kidney NAT Clontech 9010321	3.4	26.4
Normal Uterus GENPAK 061018	0.0	0.0
Uterus Cancer GENPAK 064011	14.9	0.0
Normal Thyroid Clontech A+ 6570-1	0.0	0.0
Thyroid Cancer GENPAK 064010	0.0	0.0
Thyroid Cancer INVITROGEN A302152	0.0	0.0
Thyroid NAT INVITROGEN A302153	0.0	0.0
Normal Breast GENPAK 061019	5.2	3.5
84877 Breast Cancer (OD04566)	0.0	0.0
85975 Breast Cancer (OD04590-01)	0.0	0.0
85976 Breast Cancer Mets (OD04590-03)	0.0	0.0
87070 Breast Cancer Metastasis (OD04655-05)	0.0	0.0
GENPAK Breast Cancer 064006	0.0	2.5
Breast Cancer Clontech 9100266	6.2	0.0
Breast NAT Clontech 9100265	0.0	0.0
Breast Cancer INVITROGEN A209073	1.5	2.5
Breast NAT INVITROGEN A2090734	24.3	26.2
Normal Liver GENPAK 061009	10.5	2.7
Liver Cancer GENPAK 064003	5.9	1.7
Liver Cancer Research Genetics RNA 1025	21.6	11.0
Liver Cancer Research Genetics RNA 1026	0.0	0.0
Paired Liver Cancer Tissue Research Genetics RNA 6004-T	3.3	13.5
Paired Liver Tissue Research Genetics RNA 6004-N	3.2	1.4
Paired Liver Cancer Tissue Research Genetics RNA 6005-T	0.0	0.0
Paired Liver Tissue Research Genetics RNA 6005-N	0.0	0.0
Normal Bladder GENPAK 061001	0.0	0.0
Bladder Cancer Research Genetics RNA 1023	0.0	0.0

Bladder Cancer INVITROGEN A302173	4.6	2.3
87071 Bladder Cancer (OD04718-01)	17.9	11.4
87072 Bladder Normal Adjacent (OD04718-03)	0.0	0.0
Normal Ovary Res. Gen.	0.0	0.0
Ovarian Cancer GENPAK 064008	1.7	4.8
87492 Ovary Cancer (OD04768-07)	0.0	2.1
87493 Ovary NAT (OD04768-08)	0.0	0.0
Normal Stomach GENPAK 061017	3.3	2.9
NAT Stomach Clontech 9060359	0.0	0.0
Gastric Cancer Clontech 9060395	0.0	0.0
NAT Stomach Clontech 9060394	0.0	0.0
Gastric Cancer Clontech 9060397	0.0	0.0
NAT Stomach Clontech 9060396	0.0	0.0
Gastric Cancer GENPAK 064005	6.3	3.8

Table 18: Taqman Results for clone 27455183.0.19 (Panel 4D)

Tissue_Name	Panel 4D	
	Run 1	Run 2
93768_Secondary Th1_anti-CD28/anti-CD3	0.0	0.0
93769_Secondary Th2_anti-CD28/anti-CD3	0.0	0.0
93770_Secondary Tr1_anti-CD28/anti-CD3	13.5	17.1
93573_Secondary Th1_resting day 4-6 in IL-2	0.0	0.0
93572_Secondary Th2_resting day 4-6 in IL-2	0.0	0.0
93571_Secondary Tr1_resting day 4-6 in IL-2	0.0	0.0
93568_primary Th1_anti-CD28/anti-CD3	0.0	0.0
93569_primary Th2_anti-CD28/anti-CD3	0.0	0.0
93570_primary Tr1_anti-CD28/anti-CD3	0.0	0.0
93565_primary Th1_resting dy 4-6 in IL-2	0.0	0.0
93566_primary Th2_resting dy 4-6 in IL-2	0.0	0.0
93567_primary Tr1_resting dy 4-6 in IL-2	0.0	0.0
93351_CD45RA CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93352_CD45RO CD4 lymphocyte_anti-CD28/anti-CD3	0.0	0.0
93251_CD8 Lymphocytes_anti-CD28/anti-CD3	0.0	0.0
93353_chronic CD8 Lymphocytes 2ry_resting dy 4-6 in IL-2	0.0	0.0
93574_chronic CD8 Lymphocytes 2ry_activated CD3/CD28	0.0	0.0
93354_CD4_none	5.8	0.0
93252_Secondary Th1/Th2/Tr1_anti-CD95 CH11	0.0	0.0
93103_LAK cells_resting	0.0	0.0
93788_LAK cells_IL-2	0.0	0.0
93787_LAK cells_IL-2+IL-12	0.0	0.0
93789_LAK cells_IL-2+IFN gamma	0.0	0.0
93790_LAK cells_IL-2+ IL-18	0.0	0.0
93104_LAK cells_PMA/ionomycin and IL-18	0.0	0.0
93578_NK Cells IL-2_resting	0.0	0.0
93109_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93110_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93111_Mixed Lymphocyte Reaction_Two Way MLR	0.0	0.0
93112_Mononuclear Cells (PBMcs)_resting	0.0	0.0
93113_Mononuclear Cells (PBMcs)_PWM	0.0	0.0
93114_Mononuclear Cells (PBMcs)_PHA-L	0.0	0.0
93249_Ramos (B cell)_none	0.0	38.2
93250_Ramos (B cell)_ionomycin	0.0	0.0
93349_B lymphocytes_PWM	0.0	68.8

93350_B lymphocytes_CD40L and IL-4	31.0	0.0
92665_EOL-1 (Eosinophil)_dbcAMP differentiated	0.0	0.0
93248_EOL-1 (Eosinophil)_dbcAMP/PMA/ionomycin	0.0	0.0
93356_Dendritic Cells_none	0.0	0.0
93355_Dendritic Cells_LPS 100 ng/ml	0.0	0.0
93775_Dendritic Cells_anti-CD40	32.5	0.0
93774_Monocytes_resting	0.0	0.0
93776_Monocytes_LPS 50 ng/ml	0.0	0.0
93581_Macrophages_resting	0.0	0.0
93582_Macrophages_LPS 100 ng/ml	0.0	0.0
93098_HUVEC (Endothelial)_none	0.0	0.0
93099_HUVEC (Endothelial)_starved	11.3	0.0
93100_HUVEC (Endothelial)_IL-1b	0.0	14.6
93779_HUVEC (Endothelial)_IFN gamma	0.0	0.0
93102_HUVEC (Endothelial)_TNF alpha + IFN gamma	0.0	0.0
93101_HUVEC (Endothelial)_TNF alpha + IL4	0.0	0.0
93781_HUVEC (Endothelial)_IL-11	0.0	0.0
93583_Lung Microvascular Endothelial Cells_none	0.0	0.0
93584_Lung Microvascular Endothelial Cells_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92662_Microvascular Dermal endothelium_none	0.0	0.0
92663_Microvascular Dermal endothelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93773_Bronchial epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml) **	0.0	0.0
93347_Small Airway Epithelium_none	0.0	0.0
93348_Small Airway Epithelium_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92668_Coronary Artery SMC_resting	0.0	0.0
92669_Coronary Artery SMC_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
93107_astrocytes_resting	0.0	0.0
93108_astrocytes_TNFa (4 ng/ml) and IL1b (1 ng/ml)	0.0	0.0
92666_KU-812 (Basophil)_resting	0.0	40.3
92667_KU-812 (Basophil)_PMA/ionomycin	0.0	0.0
93579_CCD1106 (Keratinocytes)_none	0.0	0.0
93580_CCD1106 (Keratinocytes)_TNFa and IFNg **	0.0	0.0
93791_Liver Cirrhosis	100.0	99.3
93792_Lupus Kidney	0.0	0.0
93577_NCI-H292	0.0	0.0
93358_NCI-H292_IL-4	0.0	0.0
93360_NCI-H292_IL-9	10.6	0.0
93359_NCI-H292_IL-13	0.0	65.5
93357_NCI-H292_IFN gamma	0.0	24.8
93777_HPAEC_-	0.0	0.0
93778_HPAEC_IL-1 beta/TNA alpha	0.0	0.0
93254_Normal Human Lung Fibroblast_none	0.0	0.0
93253_Normal Human Lung Fibroblast_TNFa (4 ng/ml) and IL-1b (1 ng/ml)	0.0	0.0
93257_Normal Human Lung Fibroblast_IL-4	0.0	0.0
93256_Normal Human Lung Fibroblast_IL-9	0.0	0.0
93255_Normal Human Lung Fibroblast_IL-13	0.0	0.0
93258_Normal Human Lung Fibroblast_IFN gamma	0.0	0.0
93106_Dermal Fibroblasts CCD1070_resting	0.0	0.0
93361_Dermal Fibroblasts CCD1070_TNF alpha 4 ng/ml	0.0	43.8
93105_Dermal Fibroblasts CCD1070_IL-1 beta 1 ng/ml	0.0	0.0
93772_dermal fibroblast_IFN gamma	42.0	27.7
93771_dermal fibroblast_IL-4	10.7	90.1
93259_IBD Colitis 1**	0.0	0.0
93260_IBD Colitis 2	13.8	0.0
93261_IBD Crohns	0.0	46.7

735010_Colon_normal	15.6	0.0
735019_Lung_none	12.9	16.8
64028-1_Thymus_none	69.3	100.0
64030-1_Kidney_none	0.0	0.0

Taqman results in Table 18 demonstrate that clone FCTR6 is differentially expressed in clear cell Renal cell carcinoma tissues versus the normal adjacent kidney tissues and thus could have a potential role in the treatment of renal cell carcinoma.

EQUIVALENTS

Although particular embodiments have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims which follow. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the invention without departing from the spirit and scope of the invention as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims.